

# RADIUM

EDITED BY

CHARLES H. VIOL, Ph. D.

AND

WILLIAM H. CAMERON, M. D.

VOL. 2, New Series

JULY, 1923

No. 2

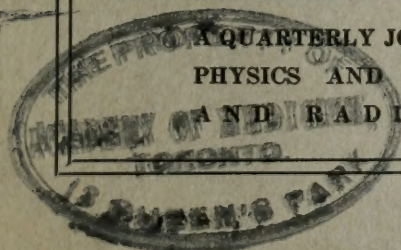
## CONTENTS

	Page
Treatment of Malignant Neoplasms of the Tonsils. Douglas Quick, M.B. (Tor.) .....	97
Effects of Irradiation on Fetal Development. Harold Bailey, M.D. and Halsey J. Bagg, Ph.D.....	109
A Skin Cancer Following Exposure to Radium. Ward J. MacNeal, Ph.D., M.D. and George S. Willis, M.D.....	119
Results of Radium in Gynecology. Alice F. Maxwell, M.D....	128
Notes on the Clinical Value of Radium in the Management of Uterine Hemorrhage. John Osborn Polak, M.Sc., M.D., F. A. C. S. ....	133
Classification and Relative Value of the Various Methods Employed for the Internal Administration of Radium Emanation and Radium Salts. William H. Cameron, M.D. and Charles H. Viol, Ph.D., .....	136
An Instrument for the Application of Radium to the Tonsils. Clarke Wallace Stewart, M.D.....	149
Radium and the Income Tax. George E. Pfahler, M.D.....	150
American Radium Society .....	176
American College of Radiology.....	176

## REVIEWS AND ABSTRACTS

The Present Field for the Use of the X-Rays and Radium in the Treatment of Malignant Neoplasms. William S. Stone, M.D....	153
The Effects of the X-Rays and Radium on the Blood and General Health of Radiologists. George E. Pfahler, M.D.....	159
Treatment of Recurrent Inoperable Carcinoma of Breast by Radium and Roentgen Ray. Burton J. Lee, M.D.....	163
A British Medical Association Lecture on the Problem of the Radium Therapy of Cancer. Arthur Burrows, M.D.....	172

THE FROM A QUARTERLY JOURNAL DEVOTED TO THE CHEMISTRY  
PHYSICS AND THERAPEUTICS OF RADIUM  
AND RADIO-ACTIVE SUBSTANCES







# RADIUM

A QUARTERLY JOURNAL DEVOTED TO THE CHEMISTRY, PHYSICS AND  
THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES

---

Copyright 1923 by Radium Chemical Co.

---

Edited by Charles H. Viol, Ph. D., and William H. Cameron, M. D., with the assistance of  
collaborators working in the fields of Radiochemistry, Radioactivity and Radiumtherapy.

---

Address all communications to the Editors, Forbes and Meyran Avenues,  
Pittsburgh, Pa.

---

Annual Subscription \$2.00.

Single Copies 50 Cents.

---

**VOL. 2, New Series**

**JULY, 1923**

**No. 2**

---

## TREATMENT OF MALIGNANT NEOPLASMS OF THE TONSILS \*

DOUGLAS QUICK, M.B. (Tor.)

Attending Surgeon, Memorial Hospital, New York City.

A review of the literature on new growths of the tonsil emphasizes several surprising features. Malignant tumors in this location are considered rare, and, with a few exceptions, reports are of individual cases. The question of diagnosis is uncertain in many reports. The opinion seems to prevail that carcinoma occupies a minor place in the entire group while a loose classification of sarcoma covers the majority of cases. In spite of its accessibility and early symptomatology the older methods of treatment have accomplished probably less here than in any of the intra-oral group of neoplasms.

In view of this it seems advisable to report on the results obtained to date with radium at the Memorial Hospital.

Because of the difficulty in deglutition, neoplasms of the tonsil are usually noted early, but, unfortunately, they rarely receive proper attention at this stage. Valuable time is usually lost in using local caustic applications followed by anti-syphilitic treatment and when these fail it is a common thing to find an incomplete tonsillectomy performed. The liberties taken with tonsillar ulcers seem out of proportion even to those taken with other intra-oral new growths. It frequently happens that a correct diagnosis is not made until the disease recurs locally or appears in the cervical nodes. The factor of error seems greatest in carcinoma of the tonsil. This is probably due to the fact that the ulcer is small and slow growing and that palpation, as a means of clinical examination, is seldom resorted to. This type of growth, however, predominates in older

---

\*Reprinted by permission from the Journal of Radiology, iii, 173-178, May, 1922.



## RADIUM

subjects, especially after the fourth decade. In young patients, lymphosarcoma is the most common neoplasm encountered. It assumes various atypical forms and hence we find in the literature many varieties of sarcoma reported in the tonsil. In fact, all of these probably belong to the group of lymphosarcomas or malignant granulomas.

The report and extensive resume made on this subject a few years

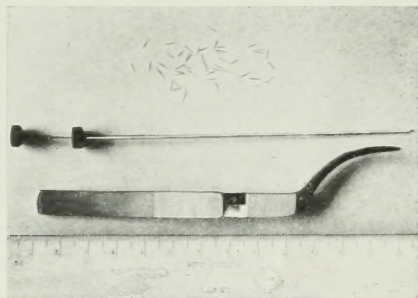


Figure I.—Unfiltered tubes of radium emanation used for insertion interstitially.

ago by Matthews <sup>(1)</sup> is most instructive. He considers practically all cases surgically inoperable and points out that, even in cases apparently localized, the prompt recurrence following surgical removal indicates that infiltration at the base is more widespread than is apparent. This is especially true of lymphosarcoma. Matthews concluded that, with the methods in practice at the time of his report, the cure of malignant disease of the tonsil was effected in only a small percentage of cases and that the operative procedures which promised most chance of cure were so

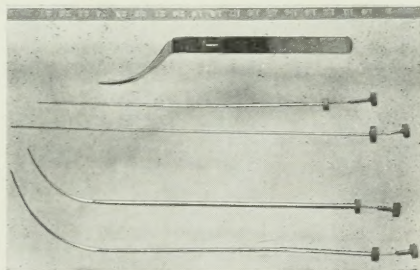


Figure II.—Trocar needles used for insertion of radium emanation tubes.

extensive as to be attended with considerable mortality. This referred especially to lateral or external pharyngotomy. Of the more limited procedures he felt that tonsillectomy was of little value but that tonsillectomy plus cauterization gave a much better chance. With tonsillectomy alone, in twenty cases of sarcoma and three of carcinoma, most presumably early and favorable cases, not one was reported to have lived two years without recurrence, and only three (all sarcomas) were reported without recurrence at periods between six months and one year. He felt that in children, especially, radical treatment was of little avail and usually detrimental. Of cases treated by tonsillectomy and cautery he found fifteen reported cases with one free from recurrence after three years. In



this group, Jacobson's (<sup>2</sup>) case is the longest reported without recurrence—eleven years. Of Matthews' own twenty-two cases, only a few of which came to operation, there were no cures. In his group of collected cases there were eighty-four of sarcoma. Of these eleven remained without recurrence six months to one year, five one to two years, six two to three years and one over three years. The case going over three years was the one treated by combined tonsillectomy and cautery. Of those between two and three years one was the result of combined tonsillectomy and cautery, four, lateral pharyngotomy, and one Coley's toxin without operation. In the collected group of twenty-three carcinomas he found one case without recurrence six months to one year, three cases one to two years and three over three years. Two of the cases over three years were by combined tonsillectomy and cautery. Coley's report in 1915 gave four cases, probably all lymphosarcoma, which remained well for periods of one to eight and one-half years following the use of his toxin alone.

Of the other operative procedures practically no good results were reported. The method of exposure by cheek splitting gave no case over two years without recurrence. This method was probably not resorted

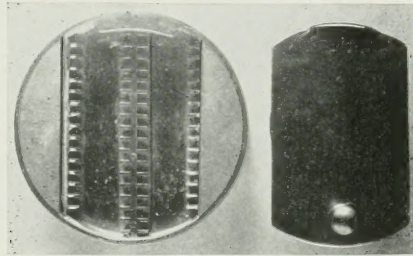


Figure III.—Two mm. brass tray to hold tubes for external application over the neck.

to, however, except in very advanced cases. Dawbarn's method of ligating both external carotids and injecting paraffin into the vessel on the affected side gave no results worth mentioning. In Jacobson's report, the cures by open mouth methods are placed at ten per cent. This rate is, however, questionable because the time interval was short and the group of cases small. Matthews noted the palliative relief afforded by x-ray in some cases. Decrease in pain and retardation of growth were the benefits observed from this agent.

Various other observers have noted the palliative effects of x-ray, but all reports are of one or very few cases and no reported complete regression is of sufficient duration to make it of statistical value.

A few isolated reports are also to be found on the use of radium, either alone or in conjunction with x-ray. In these the time interval is short, and the final results inconclusive, except in so far as they relate to palliative relief. In a number of them the radium dosage was hopelessly small. A very recent report of a case by Perrier (<sup>3</sup>) is most interesting. He reports an extensive lymphosarcoma, treated by the Janeway (<sup>4</sup>) method of burying radium emanation in tubes, both in the tonsil and cervical nodes, and clinically free from disease at the time of his report—two months after the close of treatment.

This method of treating new growths of the tonsil with radium emanation buried interstitially was first introduced in our work over five

## RADIUM

years ago by the late Doctor H. H. Janeway and has proven of inestimable value.

It has been our experience that, in comparison with other intra-oral neoplasms, those of the tonsil are particularly susceptible to radium. This may be due to the fact that in young subjects the active lymphoid tissue exerts a strong defensive force, while in later life the lack of blood supply and resultant tonsillar atrophy favors the action of radium. Once the disease has extended beyond the tonsil, however, the problem becomes more complex. The same cancer tissue seems to be influenced in its degree of malignancy by the nature of the soil in which it grows; the abund-

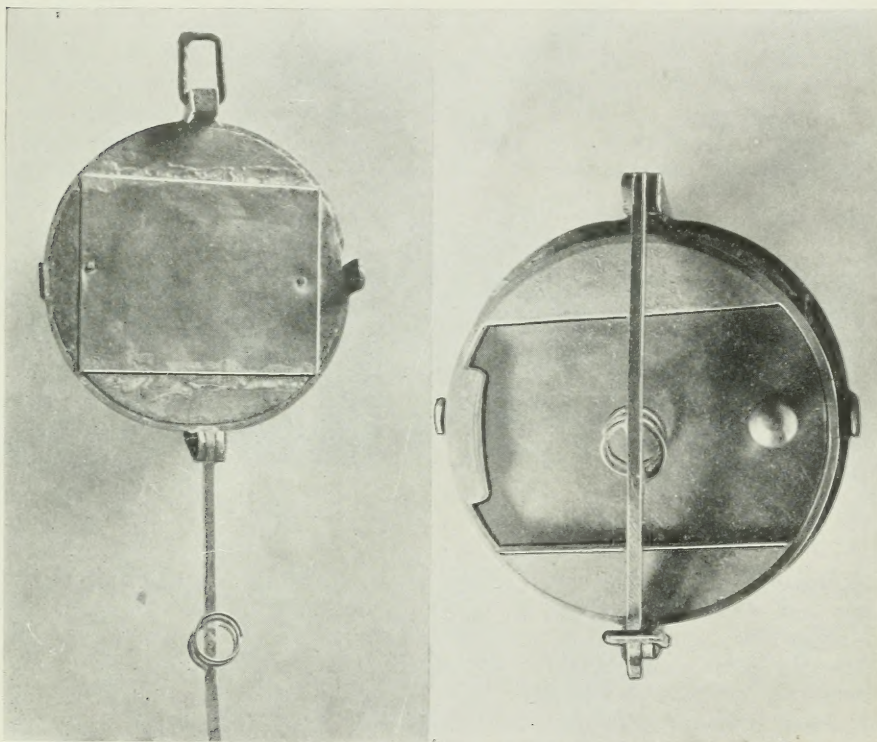


Figure IV.—Three cm. block to afford uniform separation of brass tray from skin.

Figure V.—Brass tray clamped in place on block.

ance of blood supply, freedom of movement and arrangement of anatomical planes seem to be the controlling factors in this apparent variation of growth.

As the disease advances in the tonsil one very common extension is that across the base of the anterior tonsillar pillar to the tongue. In this location it is quite as difficult to deal with as a primary carcinoma of the tongue. We feel that, in cases where this involvement is present when the patient is admitted to the service, the prognosis is only about fifty per cent as good as it would be were the disease confined entirely to the tonsil. Extension to the other adjacent structures—anterior tonsillar pillar, soft palate or lateral pharyngeal wall—is equally as complicating except in so far as the relative accessibility is concerned. In the tongue in-



filtration is deeper and more ill-defined. This is due to greater thickness of tissue, a rich blood supply and the free motion of that organ.

As for regional extension of the disease to cervical lymph nodes, we feel that this process is embolic, at least in so far as carcinoma is concerned. In view of this we have for the past few years divided the treatment of all intra-oral carcinoma into two stages—first, treatment of the primary growth, and second, treatment of the cervical nodes. In this report the same plan will be followed with exceptions made for lesions other than carcinoma.

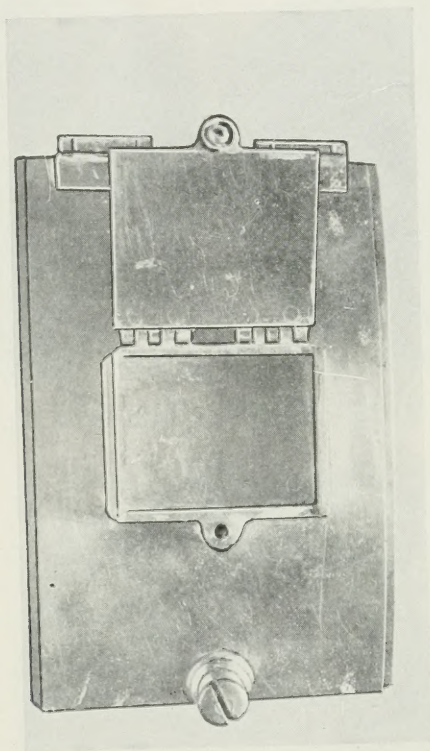


Figure VI.—Radium pack; two mm. brass filtration for application at varying distances over cervical nodes.

## I.—TREATMENT OF THE PRIMARY GROWTH

We feel very strongly that all malignant neoplasms primary in the tonsil, unless very far advanced, should be treated by radium entirely. Furthermore, a clinical classification at the beginning of treatment should be made, based on the ultimate result to be hoped for. In other words, a distinction should be made between the case with possibilities for complete regression of the disease and the other for which palliation only can be expected. Treatment should be given accordingly.

Some of the very far advanced cases should resort to medicinal measures rather than the physical agents for temporary relief.

Thorough and efficient radiation of a new growth of the tonsil designed to cause a complete regression of disease necessitates putting the patient through a painful period. Unless this complete regression can

## RADIUM

be reasonably expected, such a procedure is unwarranted. Hence the need for classification before beginning treatment. While the tonsil is readily exposed to vision, it is not so readily accessible to the older methods of radium application. Previous to 1916, when we were using only surface radiation we could do no more than give palliative relief. It is impractical to make an accurate and satisfactory surface application of



Figure VII.—Typical carcinoma of tonsil.

Figure VIII. — Typical squamous carcinoma of tonsil.

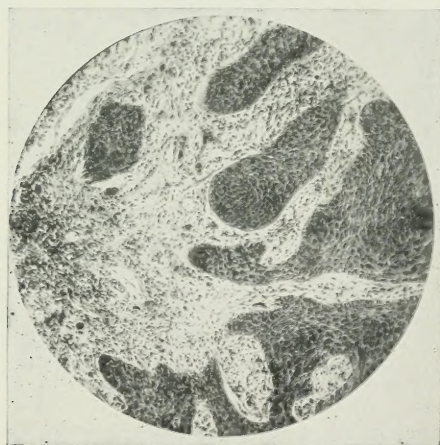


Figure IX.—Papillary acanthoma of tonsil.

radium to the tonsil for a period long enough to afford proper dosage. Even with radium tubes held in place by a hook at one end we were unable to maintain the accuracy and intimacy of application necessary for uniform results. However, as soon as we began the use of radium emanation buried interstitially our results at once improved. This method has been described several times before and needs only brief reference. Fine glass capillary tubes 0.3x3 mm. in size, containing radium emanation, are inserted at any desired depth in the neoplasm by means of trocar needles. Since this emanation decreases in value at the rate of approxi-



mately fifteen per cent per day, the total dosage to be derived from a given amount embedded can readily be calculated. The thin wall of the glass tube removes but little more than the alpha rays so that the total intensity of both beta and gamma rays is directed at the new growth. Apart from the ease of application there are several advantages in this method. Utilization of the beta radiation produces a very intense local

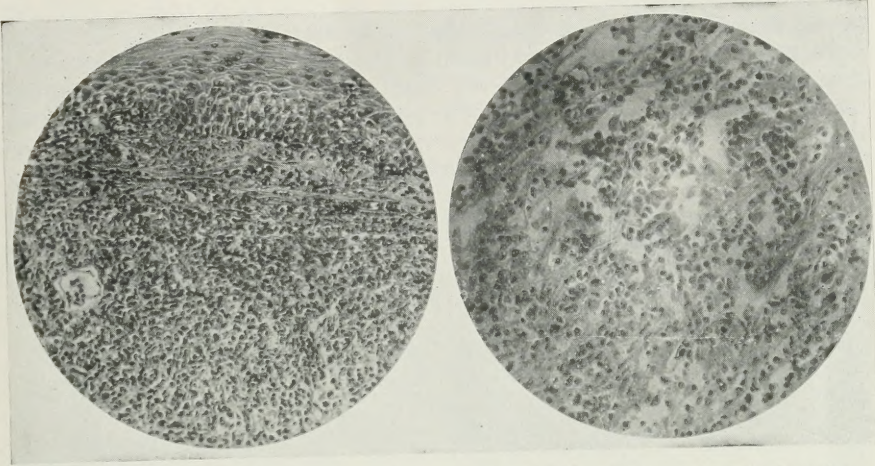


Figure X.—Lymphosarcoma of tonsil.

Figure XI.—Very cellular lymphosarcoma of tonsil.

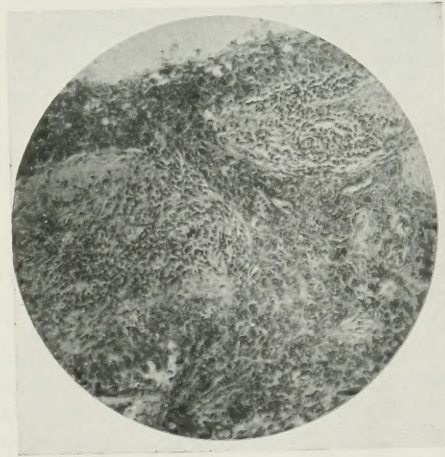


Figure XII.—Cellular carcinoma in lymph-node, untreated.

effect. The tubes are held in place by the tissues and afford an excellent cross-fire of radiation. Radiation is evenly distributed, since the tubes can be buried at any desired depth; this is especially important in reaching the actively infiltrating base of a new growth. The slow prolonged radiation permits of greater dosage and is of further significance if malignant cells are more susceptible at the time of division.

The same method can be approximated by using thin metal needles containing radium salt buried interstitially. The chief disadvantages are

the lesser amount of beta radiation obtained, the shorter exposure, smaller dose necessitated and the difficulty of retaining them in position.

We have never had trouble from the glass capillary tubes as foreign bodies. In solid tumors they become encysted by fibrous tissue excited to formation by the intense radium inflammation, while in more friable ulcerating lesions such as are usually found in the tonsil the majority of them probably slough out.

We have, however, had trouble from the amount of radium used per tube. In our earlier work with buried emanation we used tubes of three, four and even five millicuries each. These produced an unwarranted amount of sloughing with frequent resultant hemorrhages, to say nothing of the unnecessary suffering on the part of the patient. We now feel that tubes of one mc. each or thereabouts give best results. They occasion less sloughing and pain, and hemorrhage, which is still a factor to be

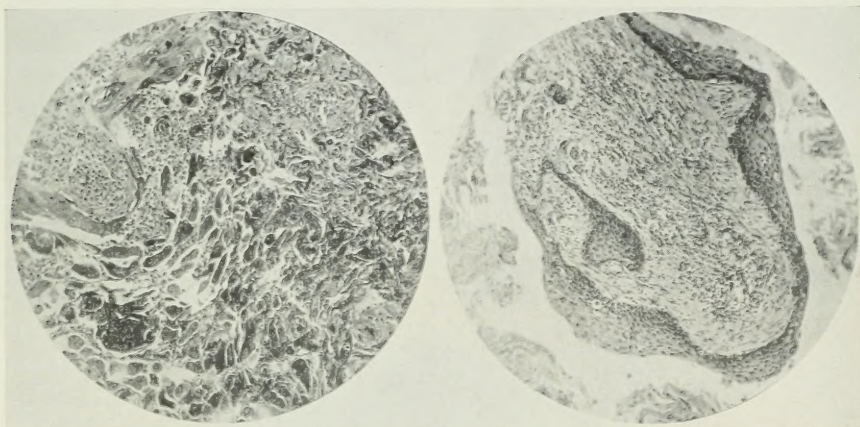


Figure XIII.—Lymph node invaded by carcinoma metastatic from tonsil, treated by heavy exter-radiation and removed surgically one month later.

Figure XIV.—Lymph node invaded by carcinoma, treated by implantation of radium emanation bare tubes and removed surgically three weeks later.

watched for carefully in tonsillar work, is much less frequently encountered. Tubes of much less than one mc. do not afford enough gamma radiation to be efficient, unless a larger number are used. This traumatizes the tissues too much. In carcinoma, one millicurie of radium emanation per cubic centimeter of tumor tissue is approximately the required dosage. With lymphosarcoma or malignant granulomas, on the other hand, about one-half this amount is all that is usually required. It is always best to aim at complete regression from a single dose. It entails less suffering on the part of the patient, and, furthermore, a subsequent dose can never be as accurately placed because of the surrounding inflammatory tissue. The amount of fibrosis following the first massive dose renders a second dose less effective and is more apt to be followed by hemorrhage from a rapid breaking down of this fibrous tissue. Wherever subsequent treatment is necessitated following an initial massive dose, the patient should be kept under close observation until all slough has separated or the external carotid artery should be ligated as a precaution.

Where treatment is to be given for palliative purposes only, much smaller amounts should be used and these can be supplemented from time to time without at any period exciting an extremely painful reaction. In



treating these advanced cases care should always be taken to prevent making them worse rather than becoming too optimistic over faint possibilities of controlling the disease entirely and pushing treatment too radically.

In introducing the emanation tubes with trocar needles, care should be taken to make the distribution as accurate as possible with the greater concentration of dosage toward the base of the neoplasm rather than near its surface. Two points are of special importance in locating the tubes. One of these is at the base of the anterior tonsillar pillar to block off extension to the tongue. The other is the lowermost part of the lesion, which is frequently just out of sight unless the indirect method is used. Failure to place the emanation properly at this point may permit exten-

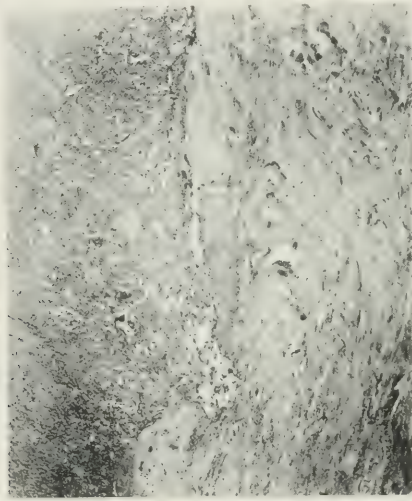


Figure XV.—Lymph node invaded by carcinoma, treated by imbedding of bare tubes of radium emanation, and removed surgically two months later. Note the complete replacement of carcinoma by fibrous tissue.

sion of the disease to the lateral pharyngeal wall or the extreme base of the tongue before it is recognized. In order to introduce the tubes more accurately here we use curved trocar needles and introduce them by the indirect method.

In the cases of recurrent new growths of the tonsil, which, unfortunately, we see only too frequently, the problem is very much altered and recurrence or implantation is usually at the periphery. In these cases the emanation tubes must be placed very widely.

The question of trauma must always be considered in using emanation tubes interstitially. Whenever possible a surface application of filtered radium should be used a few days before introducing the tubes. In the tonsil, this can be done very efficiently by placing heavily filtered radium over the tonsillar area, externally. Our own plan is to use two thousand to twenty-two hundred millicurie hours filtered by two mm. of brass and placed three mm. from the skin surface just posterior to the angle of the mandible. We feel that this renders emboli due to trauma much less harmful, thereby relieving in large measure the danger of introducing the trocar needle.

## II.—TREATMENT OF THE CERVICAL NODES

Since this phase of the work has been recently dealt with <sup>(15)</sup> in considering the treatment of the neck in all cases of intra-oral carcinoma, only brief mention of it will be made here.

Because of our belief in the embolic theory of extension of carcinoma to the cervical nodes, we have adopted an expectant plan of treatment, or rather, a combination of radiation and conservative surgery.

As soon as a case enters the service x-ray is applied to both sides of the neck and a heavily filtered tray of radium is placed over the tonsillar region, externally. If a definitely enlarged node is present in the neck the radium ray is used over this also. If the neck is free from palpable involvement, x-ray is repeated at intervals over a period of several weeks. If surgically operable nodes are present at first, or appear subsequently, a 'complete unilateral block-dissection' is done under local anaesthesia, two to six weeks following the external radiation, and radium emanation is buried at all suspicious points in the wound, especially where the lymphatic channels are severed. If the nodes be extensively involved in the beginning or are found at the time of operation to have invaded their capsule, no attempt is made to remove them, but emanation tubes are buried uniformly throughout the mass. We feel that it is best to expose such nodes surgically before burying the emanation because of the altered anatomy and because the tubes can be more accurately placed.

While external radiation produces marked inhibitory changes we have never seen complete destruction of epidermoid carcinoma metastatic in the cervical nodes from its use alone. On the other hand, we now have a small group of cases showing complete regression following the burying of emanation throughout the nodes in the manner just described.

In all cases where the neck structures are exposed surgically the external carotid artery on the side of the primary lesion should be ligated to prevent hemorrhage unless the primary site is entirely healed.

In dealing with the cervical extensions of lymphosarcoma or the malignant granulomas the physical agents alone should be used. Preferably this should be by a combination of x-ray over the surface and radium emanation interstitially. It should be stated most emphatically that surgery plays no part in the treatment of this group.

## STATISTICS OF TREATED CASES

During the past five years we have treated one hundred and forty-nine cases of malignant neoplasms of the tonsil.

Many of these were very advanced cases, frequently recurrent after operation, and as we review the work three errors must be recognized, especially in the early part of the series. A large group of cases were so advanced that I am convinced they would have been better off had no radium been used. There comes a time in the course of the disease when medical measures give more relief than the physical agents. Some cases which should have been classified for palliative treatment only were treated too vigorously in the hope of obtaining a complete regression of disease. In these, the treatment defeated its own purpose. In our earlier work with buried emanation the tubes used were for the most part too strong so that an unnecessary amount of suffering was produced to obtain a result which can now be attained with more comfort and less danger.



Our present follow up of these cases shows the following results. Of one hundred and twenty-four cases of carcinoma of the tonsil, twenty-eight cases are now clinically free from disease. Two other cases were free from clinical evidence of disease for fifteen months, at which time they were lost track of. Twenty cases at present under treatment are progressing favorably and a fair number at least bear promise of a complete clinical regression.

Forty-one cases were definitely improved for varying periods of time, but finally either died of the disease or are steadily becoming worse. Improvement in these cases means slowing up or definite regression of the growth, relief from pain, reduction in size of cervical nodes or prevention of their breaking down and fungating externally. Twenty-seven cases were absolutely unimproved by treatment and ten more were completely lost track of, so that they must be classified with those totally unimproved. Of the carcinomas, ten were recurrent cases, two of which were with recurrent cervical nodes and an unrecognized primary lesion in the tonsil.

Twenty-four cases belonged to the group of lymphosarcomas or malignant granulomas. It is my impression that a few more cases belonging in this group are filed under the general heading of lymphosarcoma and hence were inaccessible for this report. Of this group six cases are now free from clinical evidence of disease. One shows an excellent palliative result of over three years duration, but at no time has he been entirely free from clinical evidence of disease. Six of these cases were recurrent.

One case of rhinoscleroma of the tonsil is of interest. The patient has been under treatment for over three years, at times showing an apparent complete regression, only to reappear in some adjacent area of mucosa.

Of the twenty-eight cases of carcinoma of the tonsil reported clinically free from disease at present, the average duration since the initial treatment is twenty-six months. The longest period is fifty-six months and the most recent four months. In ten cases, neck operations, as previously described, were performed and in these the average duration is twenty-eight months. The oldest is fifty-six months and the most recent six months.

Another case, of interest from a palliative standpoint, was admitted eighteen months ago with an advanced primary growth and metastases in both sides of the neck. This patient has been treated by burying emanation, entirely, and while he has not a complete regression, there is nevertheless complete temporary control and no subjective symptoms. This case is cited simply as an example of palliative relief.

Of the lymphosarcomas or closely allied lesions one case has had a complete regression for over four years, another sixteen months, one twelve months, one eight months and two six months. Another case was lost track of a year and a half after treatment with complete regression at that time. One of the most interesting cases in this group is a patient in whom the tonsillar lesion cleared up promptly, but a large mass appeared in the neck and another in the lower left quadrant of the abdomen. Under heavy radiation these reduced somewhat and have remained stationary and quiescent without treatment for two years. His initial treatment was over three years ago.

In general, lymphosarcoma, because of its extremely cellular structure, responds very promptly to radium and the area treated tends for

the most part to remain well, but dissemination is early and widespread and it is doubtful if many permanent results can be hoped for from radiation of the local process.

#### CONCLUSIONS

1. In all malignant neoplasms of the tonsil, radium is the agent of choice for treatment of the primary growth.

2. Best results can only be obtained in these cases by interstitial radiation—either by means of radium emanation or lightly filtered needles containing radium element embedded in the growth. This should be supplemented by heavily filtered external radiation—either x-rays or radium.

3. The treatment of cervical metastases of carcinoma of the tonsil is best managed by a combination of radium, x-ray and conservative surgery.

4. In lymphosarcoma or the malignant granulomas of the tonsil, surgery plays no part whatever. Metastases to the cervical nodes or elsewhere should be managed entirely by a combination of radium and x-rays.

Our experience with this group of cases encourages us to continue the plan of treatment along these lines.

#### BIBLIOGRAPHY

- 1—Matthews, I.: Malignant Tumors of the Tonsil. *Laryngoscope*, 1912, xxii, 727-752.
- 2—Jacobson, N.: Malignant Disease of the Tonsils. *Ann. Surg.*, 1901, xxxiii, 280-298.
- 3—Perrier, C.: Lymphosarcoma of the Tonsil Treated with Radium. *Revue Medicale de la Suisse Romande*, October, 1921, xli, p. 10.
- 4—Janeway, H. H.: Treatment of Cancer, Particularly of the Tongue, Tonsil and Rectum by Buried Emanation. *Am. Jour. of Roentgenology*, Vol. vii, p. 92, February, 1920.  
Radium Therapy in Cancer at the Memorial Hospital, Paul B. Hoeber, N. Y., 1917.
- 5—Coris: Pharyngectomie Pour Lymphosarcoma de l'Amygdale. *Jour. de Chir. Bruxelles*, 1911, xi, 12-13.
- 6—Watson, W. P.: Case of Lymphosarcoma of the Tonsil and Palate. *Bristol Med. Chir. Jour.*, 1920, xxxvii, p. 51.
- 7—Goodale, J. C.: Lymphosarcoma of the Tonsil. *Boston Med. and Surg. Jour.*, 1908, clix, 409.
- 8—McCoy, John: Surgical Treatment of Cancer of the Tonsil with a Report of Cases. *Laryngoscope*, 1919, xxix, 422-424.
- 9—Canuyt, G.: Epithelioma de l'Amygdale Gauche. *Rev. Laryng. Otol, et Rhinal.*, 1918, xxxix, 12-17.
- 10—Freudenthal, W.: A Case of Sarcoma of the Tonsils Treated with Radium. *Cure. Internat. Jour.*, 1908, xxi, 12-13.
- 11—Harris, T. J.: Neoplasm of the Tonsil, Probably Malignant, Treated by the X-Ray with Apparent Benefit. *Laryngoscope*, 1906, xvi, 220-222.
- 12—Edling, L.: Sur un Cas de Sarcome de l'Amygdale traite par les rayons X et par le Radium. *C. R. Congres Internat. Physiotherapie*, 1911, 685-687.
- 13—Anchutz: Demonstration eines mit Radium Bestrahlten Tonsil



- Lencarcinoms. Verhandl. Verein Deutch. Laryngol, 1914, xxi, 332-335.
- 14—Bertolotte, M.: Sopra un caso di Carcinoma Della Tonsille Guarito Colla Rontgen-radium-therapic; Radiologica Medica. 1915, ii, 155-164.
- 15—Quick, Douglas: The Conservative Treatment of Cervical Lymphatics in Intra-oral Carcinoma. Jour. A. M. A., August 6, 1921, Vol. lxxvii, pp. 436-441.  
Treatment of Carcinoma of the Tongue. Annals of Surg., June, 1921.
- 16—Coley, Wm. B.: Primary Neoplasms of the Lymphatic Glands, including Hodgkin's Disease. The Transactions of the American Surgical Association, 1915.

## EFFECTS OF IRRADIATION ON FETAL DEVELOPMENT\*

BY HAROLD BAILEY, M.D., AND HALSEY J. BAGG, PH.D.

Memorial Hospital, New York

In the last five years radium has become available in certain amounts to many individual operators. At present there is hardly a community of any size that has not at least the equivalent of 100 mgm. of the metal. The dissemination of this active physical agent has resulted in its employment in clinical gynecological conditions as an adjunct to or in place of surgery, by many physicians who have little knowledge of the physiologic and biologic principles involved.

There have been so many loose statements concerning the cure, by irradiation, of gynecologic conditions, during all periods of sexual life, with the intimation that no serious results follow in the treatment of these conditions, that we deem it a proper time to present some clinical and experimental facts relating to this subject, especially in regard to the reaction of the ovary and the developing fetus.

In the treatment by irradiation of fibroids and myopathic hemorrhage there is still a difference of opinion as to whether the action centers mainly in the ovaries or the uterus. Many operators believe that in the treatment of fibroids the radium rays affect mainly the growth itself rather than the ovary; while in the treatment of hemorrhage, menstruation is checked by inhibiting ovulation. Notwithstanding these different views the source of irradiation is usually placed in the same place during treatment, that is, the body of the uterus. This question is so well debated that there are now two schools of thought, as Beclere<sup>1</sup> has recently pointed out. The Germans believe the radiation effect is mainly on the ovaries, while the French believe it is upon the uterus.

This is really a serious matter because of the differences in treatment that might ensue. The uterus is many times invaded and an operation of more or less magnitude is performed, where the result might be accomplished by external irradiation.

Granted that some form of irradiation is indicated in these pathologic conditions certain questions are immediately raised: Is the effect upon menstruation permanent in women irradiated during sexual life?

\*Reprinted by permission from the American Journal of Obstetrics and Gynecology, v, 461-473, May, 1923. Read at a meeting of the Section on Obstetrics and Gynecology at the Academy of Medicine, February 27, 1923.

If not, do the follicles ever regain perfect development with full capacity of forming a normal fetus?

There is another problem in this field which, in the light of recent experimental work upon animals, needs consideration. This concerns the effect upon the developing child of irradiating the fetus *in utero*. Even when the fetus is born at term and apparently of normal weight and size, do we know whether its postnatal development will be normal? The great practical importance of these questions is evident, for a review of the experimental work on the lower animals has shown that if the irradiation occurs very early in pregnancy the fetus may be so injured that it dies and is aborted, or its development may be only slightly arrested, and yet while it may be born alive, it may show great abnormalities. On the other hand, if the radiation be given late in pregnancy, the results may be of such an insidious nature, even possibly endocrine in origin, that a normally appearing offspring at birth may be stunted and show disturbances of metabolism later in life.

The results of the experimental studies in this field are conclusive in agreement that detrimental disturbances occur in animals that are exposed to a sufficient amount of irradiation during the various stages of development. This is probably due to an arrest in the orderly sequence of embryonic processes, and the type of resulting monster is apparently determined by the developmental period at which the exposure is given. Abnormal structural changes following arrested development are not all limited to the effect of irradiation. Stockard's experimental work on the production of twins, double monsters, etc., has shown that many physical and chemical agents may bring about such changes.

#### DISTURBANCES IN ANIMAL DEVELOPMENT PRODUCED BY RADIUM IRRADIATION

The brief report of the following studies deals with abnormalities produced in animal development by exposure to radium rays during the various stages of growth. Bohn<sup>2</sup> in 1903 was among the first to report maldevelopment in the sea-urchin following exposure of the eggs to radium rays, and similar reactions were noted by Perthes<sup>3</sup> for the treated ova of ascaris. Studies on amphibians have been conducted by several investigators, but the work of P. Hertwig,<sup>4</sup> O. Hertwig<sup>5</sup> and G. Hertwig<sup>6</sup> are classics in this field. Their investigations confirmed the idea that retardation of embryonic development was a sequel to irradiation. Normal fertilized ova when irradiated produced deformed larvæ, and the degree of destructive changes varied with the amount of radium used and the duration of the exposure. Interesting results were noted when normal eggs were fertilized by irradiated spermatozoa. Heavily irradiated spermatozoa produced apparently normal young, for in this case the paternal elements merely initiated what might be called a parthenogentic development, and were too extremely injured to combine their chromatic material with that of the maternal nucleus, while slightly irradiated spermatozoa produced variously deformed young. Schaper<sup>7</sup> found similar changes occurring in other amphibians treated with radium rays and Tur<sup>8</sup> reported the presence of deformities in the embryos of birds irradiated through the shell of the eggs. Bagg<sup>9</sup> has recently reported disturbances in development produced by radium emanation, and in these experiments amounts of radium emanation were used equivalent to one and one-half grams of radium metal. Clinical applicators were employed and two millimeters of lead and one-half millimeter of silver filtration ensured mainly a gamma-ray type of



radiation. Pregnant rats when irradiated near the end of pregnancy produced offspring that either died about ten days after treatment, or if living after this period, the young showed markedly deformed brains with practically no cerebral cortex, and in addition, the animals were blind and sterile in both sexes. Solutions of the active deposit of radium emanation were also used intravenously or subcutaneously in pregnant animals( the usual dose was 5 millicuries), and either produced death and absorption, or abortion of the young, or characteristic subcutaneous areas of extravasation in the developing embryo. Similar cutaneous lesions were also noted in three different litters where the mothers were treated several days before mating with untreated normal males.

## DISTURBANCES IN ANIMAL DEVELOPMENT PRODUCED BY X-RAY IRRADIATION

The results of the biologic effects of x-ray exposure on animal development closely parallels those of the radium experiments. Perthes<sup>10</sup> noted monstrosities in the embryos of ascaris exposed to x-rays. Bordier<sup>11</sup> produced abnormalities in silk worms when treated in the same manner, and Hastings, Beckton and Wedd,<sup>12</sup> working with the same species, noted a progressive loss of fertility in the insects, which was especially marked in the immediate descendants of the treated individuals. Mavor,<sup>13</sup> who has recently reported experiments on the x-ray effects on the fruit fly, *Drosophila*, has apparently shown that x-rays may produce a specific modification of the hereditary mechanism which is inherited as such. He found that a considerable number of exceptional daughters were obtained by submitting the mothers to x-rays before mating. A large proportion of these exceptional daughters has been found to be fertile and have bred further exceptions without having been submitted to x-ray. The work of Gilman and Baetjer<sup>14</sup> with amphibians showed that when the ova of *Amblystoma* were exposed to x-rays there was an apparent acceleration in development for a short time, yet the resulting offspring were abnormal. Baldwin,<sup>15</sup> also working with frog larvae, has recently reported the production of monsters conforming to a definite type by means of x-ray irradiation. Hippel and Pagenstecher<sup>16</sup> treated pregnant dogs with x-rays (twenty-one Holzkecht units were used) and produced either cataracts in the eyes of the young or death and abortion of the embryos. Regaud, Nogier and Lacassagne<sup>17</sup> noted that x-ray exposure led to abortion in dogs. Cohn,<sup>18</sup> Lengfellner,<sup>19</sup> Krukenberg,<sup>20</sup> and also Walter<sup>21</sup> report deleterious effects in animals exposed to x-rays before birth (irradiation of mother), or soon after birth. Hansen<sup>22</sup> has recently x-rayed pregnant rats and reported results very similar to those obtained by Bagg with radium. Sterility, eye defects, and deformed skulls were noted in the offspring of irradiated animals. Little and Bagg<sup>23</sup> have again reported disturbances in the offspring of mice irradiated with x-rays. Deformities of the legs, feet, head and eyes were especially noted. Their most interesting result consisted of a pronounced eye deformity, which apparently behaves in its inheritance as a Mendelizing character, and is recessive to normal. This abnormal character has been studied through seven generations of animals, and over three hundred abnormal animals were noted. Its inheritance has been tested not only by matings within the x-rayed lines, but by an outcross, and by its transmission through the males only.

During the writing of this paper we have received a reprint of

experiments recently published in France by Lacassagne and Courtard,<sup>24</sup> concerning the irradiation of rabbits with x-rays\* and the attending disturbances in the physiologic activity of the ovary, as well as marked disturbances in the later-developing fetus. When pregnant rabbits were irradiated at nearly full term with x-rays, the young treated *in utero* died at, or a short time after birth, showing pathologic reactions typical of those already described by other investigators. The experiments were mainly concerned, however, with the later sexual activity of the females that had lost their first litters. When they were mated with normal males the following results were noted:

1. Temporary sterility extending over three to four months.
2. Re-established fertility, but associated with a reduction in the number of viable young of the successive litters, frequently alternating with an apparently normal oestrus, acceptance of the male, but without fertilization being established.
3. Progressive premature sterility.
4. In certain cases the uterus was ruptured during pregnancy, and other pathologic conditions were observed that had never been seen in the control stock.
5. There were relatively few young born from irradiated females, but some of these were apparently normal, and when mated with normal males produced apparently normal offspring. However, in this group other offspring of irradiated females, although apparently normal at birth from external appearance (and later from microscopical examination, also normal), showed marked metabolic disturbances at the time of weaning, when changing from one type of food to another, and died in all cases a few days of persistent diarrhea, which was a characteristic symptom.

#### CLINICAL STUDIES SHOWING THE EFFECTS OF X-RAY AND RADIUM IRRADIATION ON HUMAN DEVELOPMENT

There are several reports by clinicians indicating that irradiation is not harmful to fetal development, but for the most part these articles deal with few cases and generally the authors are careful to qualify their statements.

Corscaden treated three women for fibroids or menorrhagia, and in a private communication to us gives the details of two cases where pregnancy followed. One woman, twenty-five years of age, was treated for bleeding, and was given an x-ray treatment equal to two-thirds of a standard sterilizing dose for a woman near the menopause period. Menstruation became more or less normal. Three years later she became pregnant and gave birth to a normal child, which to date (three years) is apparently physically normal. The second woman was thirty-eight years of age and was treated for fibromyoma, eight cm. in diameter. Fifty mg. of radium bromide were placed in the uterus for twenty-four hours. Three or four menstrual periods were missed before pregnancy was noted. When the gestation had advanced to the sixth month, miscarriage occurred, the patient giving the history of a fall. The fetus was macerated but apparently well formed. In a recent article Corscaden<sup>25</sup> concludes that normal pregnancy is possible after temporary menopause.

\*The entire abdominal region was treated. Target-skin distance 25 to 32 cm. 6 mm. of aluminum filter; 2.2 to 3.5 milliamperes; spark-gap 25 cm. The time of exposure varied from 30 to 90 minutes.



Steiger<sup>26</sup> in 1921 had a patient, thirty-nine years of age, with a fibroid uterus and exophthalmic goiter. Following the irradiation of both thyroid and uterine growths with x-ray the patient had amenorrhea. Two years later she became pregnant and was delivered at term of a well-formed, strong child. The author concludes that, despite radiation of the ovaries, a woman may become pregnant and have a normal child.

Field<sup>27</sup> describes a case of pregnancy complicated by cancer of the uterus, which he treated by irradiation. The treatment began when the fetus was in the sixth month and large doses of radium were employed during this period, making a total of 7,320 mg. hours. Seven weeks after the first dose premature labor occurred, with the delivery of a four pound infant which was normal and remained so, but was followed only to the age of three years.

Polak<sup>28</sup> in 1922, in "Notes on the Clinical Value of Radium in the Management of Uterine Hemorrhages," found that the average dose was 400 mg. hours in the 31 cases that he treated. Six of these women are now married and two have become pregnant, and he states that it is a "fact which answers some of the criticisms which are made of using radium in young girls."

Schmitz in discussing Maury's paper<sup>29</sup> on the "Results of the Exposure of Animal Ovaries to the Rays of Radium," states that he had two patients whom he treated for uterine bleeding, and who later became pregnant and delivered infants which were perfectly normal.

Horner<sup>30</sup> in an article on "Roentgenography in Obstetrics," states that in the use of x-ray for the purpose of determining the pelvic measurements during pregnancy there is no single instance of maldevelopment either physical or mental occurring in his series. He states that thousands of women have been subjected to x-rays during the early months of pregnancy without effect on the ovum. However, he amplifies the statement by saying, "I do not mean to imply that the x-ray cannot kill an ovum, but refer to the use of the apparatus for diagnosis. The modern abortionist uses it to kill." In regard to the amount of x-ray exposure that may be used on a pregnant woman, he describes a case of his own where a total of twelve exposures amounted to 3,000 milliamperes seconds.

J. G. Clark and F. B. Black<sup>31</sup> state, in April, 1922, in a paper on "Radiotherapy of Non-malignant Menorrhagia," that excessive menstruation may be regulated with a fair degree of certainty, and they do not hesitate to use irradiation in urgent cases even in pubescent girls. They further state "moderate exposure may kill only the older and riper follicles that are near the surface (of the ovary), while the younger and less developed bodies escape its influence."

The following clinical reports record harm to the fetus following irradiation or, at least, indicate the need of caution in treating before or during gestation.

In August, 1922, J. G. Clark and F. E. Keene<sup>32</sup> analyzed 527 cases of myoma uteri and myopathic lesions, and state that in adolescent girls one should be most wary in using radium because in sufficient dosage it will just as surely stop menstruation for all time as will double oophorectomy. They show a preference for operation rather than radium in the treatment of young women with fibroids. In regard to pregnancy following irradiation, their experience consisted in the treatment of five women. The authors state that the application of radium gives but little forecast in favor of restoring the child-bearing

possibilities. There were seven pregnancies in this group of women, three infants were born at term and four miscarriages or premature deliveries were noted, three occurring in one patient.

Archangelsky<sup>33</sup> reports the results from treating ten women suffering from tuberculosis where termination of pregnancy was necessary. They were given x-ray irradiation over six abdominal and two dorsal fields. The dose varied from eighteen to sixty-seven Holzknecht units. Both German and American tubes were used, and one mm. of aluminum filter and two mil. amp. of current. Three to seven treatments were given. Seven of the ten cases were treated when not more than two months pregnant, while three were slightly more advanced. All of the seven cases showed considerable bleeding, apparently as a result of the irradiation, there was complete abortion and three embryos were found after expulsion. Abortion did not occur in the three women with slightly older pregnancies (only one showed some slight bleeding after irradiation), surgical intervention was necessary and revealed in each instance a dead embryo. Histologic examination of each of these embryos showed destructive changes in the central nervous system. It is interesting to note that the dosage employed was not sufficiently strong to prevent the prompt return of menstruation in all the women, with one again becoming pregnant. The author concludes that x-ray irradiation should not be considered as ineffective in the treatment of pregnant women, and that he had especially demonstrated that deleterious effects on the fetus and abortion would result from irradiation during the first days and weeks of pregnancy.

Stacy<sup>34</sup> in the treatment with radium of 1013 cases of menorrhagia reported the occurrence of ten pregnancies following the treatment. Four normal infants were born and three were dead at birth. One woman had two miscarriages and another was pregnant at the time of the report. Stacy concludes that small doses of radium are indicated in a few selected cases of menorrhagia of young women of the child-bearing age.

Berkley,<sup>35</sup> in reporting a case where cesarean radical hysterectomy followed the application of radium to the cervix in a pregnant woman, states that a child was born, which was apparently normal up to seven years and five months after birth. Two hundred and thirty-two mg. were placed in the cervix for eight hours during the sixth and seventh month of pregnancy, and cesarean section followed at nearly full term. The interesting observation in this case is that according to the author the baby at birth had two bald patches on its head corresponding to the position that the radium had occupied. These bald spots disappeared later on.

Stettner<sup>36</sup> reports a case of myoma accompanying pregnancy that was treated by roentgenotherapy. The child born at term showed deformed ears, eyes and genitals and also a general disturbance of co-ordination. At the age of two years this infant's mental functions were not normal. The symptoms at this time were those both of inflammatory origin and of developmental defects. The growth in height was sixteen months below normal and the ossification fourteen months behind.

Aschenheim<sup>37</sup> reports the case of a woman who was irradiated with x-rays for uterine myoma and the conception occurred between treatments. The delivery was premature at the eighth month of gestation and the child later became an imbecile. The boy had sunken and flat,



nearly blind eyes. He had a microcephalic head and occasionally had convulsions. His hearing was normal.

One of the most interesting articles on this subject is by Werner.<sup>38</sup> In 1921 he reported the results of pregnancy in seventeen women out of 1500 whom he had treated with irradiation for menorrhagia and myoma. There were twenty-four pregnancies, of these, nine were abortions; fourteen children were born alive and of these fourteen, four died within the first year. Three children, when six to eight years old, were 16 per cent below the normal in weight and 8 per cent below normal in height. There were two cases that were treated during pregnancy. In one the child was normally developed at the time of delivery. In the second case the child was born at term and weighed only two kilograms. It was lacking in fat and its skin was a pale yellow. At the time of the report the child was three years old, but its height and weight correspond to that of a two year old child, but it is otherwise healthy. Werner concludes that radiation of the ovum or the embryo may cause injury which can be followed by extensive improvement in the course of later development.

#### DESCRIPTION OF OUR CASES

Pregnancy following irradiation, or irradiation of women already pregnant.

#### IRRADIATION DURING PREGNANCY

Case 1. K. A., No. 28018. Age twenty-three years. Admitted September 10, 1920, with diagnosis of glioma of the spinal cord. This patient had previously been irradiated for the purpose of x-ray examinations of the spine on the 20th and 23rd of August. On admission she was about three and one-half months pregnant. She was treated in the intrascapular regions with 75,706 millicurie hours of gamma-ray irradiation. She was admitted to the Manhattan Maternity Hospital and on February 11, 1921, the abdomen was opened without general anesthesia and the infant was removed. It was living and had a spina bifida and double club feet. The mother died ten days later and the infant was taken to another hospital where it died after fifteen days.

Case 2. M. A., No. 27329. Age thirty-five years. Admitted to the hospital when pregnancy was six and one-half months advanced, with an epidermoid cancer of the cervix. She was treated by the insertion of "bare tubes" of radium emanation and a platinum tube of radium on February 16 for a total of 2356 millicurie hours. The following day she received 960 millicurie hours in the region of the cervix, in three directions, by means of the "bomb" applicator. She received also 297 millicurie hours in "bare tubes" placed in the cervix. Eclampsia developed and she was delivered by a cesarean section performed April 3, 1920. It was found that the breech was in the lower uterine segment. The baby had no apparent malformations. The woman died on April 16. The baby weighed  $4\frac{1}{2}$  pounds at birth and at the end of fifteen days was transferred to the Babies Hospital. It left there on May 15—forty-two days old and apparently normal, but it died of pneumonia at the age of two and one-half months.

Case 3. M. B., No. 27758. Age thirty-seven years. Epithelioma of the vulva. Patient was first seen June 12, 1920. She was then five months pregnant. She was treated with 1065 millicurie hours in "bare

tubes" implanted in the tumor. On August 15, 396 millicurie hours of bare tubes were placed in either groin after gland dissection. On September 27 she received a treatment of 2,003 millicurie hours by the so-called "block" application against the vulval tumor. The patient was transferred to the Woman's Hospital for delivery, as she had been sent to us originally by that institution. A normal infant was born by cesarean section on October 25 and is now living and apparently normal. The mother died on February 6, 1921.

#### PREGNANCIES FOLLOWING IRRADIATION

Case 1.\* B. L., No. 24298. Age twenty-five years. The patient was suffering with Hodgkin's disease and was treated by x-ray irradiation to the neck, groins, back and axilla during May and December, 1917. The woman became pregnant, and in September, 1918, she delivered a male infant which died eleven hours after birth. It had malformation of the head and the sagittal suture was open exposing the brain. The patient died two years later. Autopsy showed, among other pathologic conditions, atrophy and fibrosis of the breast and fibrous atrophy of the ovaries.

Case 2. G. W., No. 25167. Age thirty-one years. This patient was irradiated for a fibroid of the uterus. A silver wire applicator was placed in the uterus for a treatment of 420 millicurie hours, and an external application of gamma-ray irradiation was made over the uterus, at 4 cm. distance, for a total of 3005 millicurie hours. One and one-half years later she was delivered of a large, stillborn infant, weighing nine pounds and two ounces but there is no accurate information as to the cause of death.

Case 3. J. R., No. 28743. Age twenty-eight years. This patient had a fibroid uterus about the size of an orange. She had a normal child three years of age. On February 2, 1921, she was treated with radium emanation in a platinum tube, with a half millimeter of filtration, for a total of 1,000 millicurie hours. It was expected that this treatment would cause permanent sterility, but although the menstrual flow has diminished it was never entirely stopped, and in November, 1921, the patient became pregnant. On the eighth of the following August a baby was born, apparently normal, and weighing seven pounds and one ounce.

#### DISCUSSION AND SUMMARY OF RESULTS

We have attempted in this paper to bring together the experimental and clinical studies relating to the effects of radium and x-ray irradiation upon the functional activity of the ovary and the reaction upon the developing fetus, when irradiation is given before or during the various stages of pregnancy.

As previously stated in detail, the experimental data upon the lower animals have shown that when the sex glands are sufficiently irradiated *before* fertilization the following are typical fetal reactions:

1. Disturbed, abnormal, arrested development, resulting in the formation of monsters conforming more or less to a general type, and pronounced disturbances in the development of the central nervous system (Bohn, Perthes, O. and G. Hertwig, Schaper, Tur, Bordier and Baldwin).

\*We acknowledge our indebtedness to Dr. W. S. Stone for the privilege of recording this case.



A marked tendency to a progressive loss of fertility.

3. A specific modification of the hereditary mechanism (Mayor) and the production of inherited defects in the young, especially in the eyes (Little and Bagg).

Irradiation during pregnancy produces the following typical disturbances in fetal development, depending upon the developmental period at which the irradiation is instituted:

1. Disturbed, arrested, abnormal development with death of the embryos, absorption or abortion, stunting in growth, cataract, sterility, lesions of the central nervous system and blood vascular disturbances in the embryos. (Hippel and Pagenstecher, Regaud, Nogier and Lacassagne, Lengfellner, Krukenberg, Cohn, Walter, Bagg, Hansen, and Lacassagne and Coutard.)

When we come to a discussion of the clinical reports it must be borne in mind that the data cannot be presented with the same scientific evaluation that may be given to experimental biologic studies, and although we realize that one cannot directly transfer the experimental results from animal to man, yet we believe that there is no reason for considering human developmental processes as essentially different from those of other mammals, and it has been our aim to bring together the clinical reports to interpret and correlate them as much as possible, and to add our six cases. We are fully aware that developmental disturbances are to be found in many instances of human ontogeny where irradiation of women during the child-bearing period with a view to preserving the procreative ability.

In judging the clinical reports we believe that in those instances where comparatively great disturbances have resulted in the child, the irradiation was given early in pregnancy. Here we would place the children with subnormal mentality and other defects reported by Aschenheim and Stettner.

We believe that irradiation during early pregnancy may produce death and abortions of the fetus, and we would place in this group the four abortions reported by Clark and Keene, two by Stacy and nine by Werner.

Irradiation during late pregnancy is not so likely to produce gross developmental abnormalities in the child at birth, but the clinical data seem to agree with the experimental in several instances where children irradiated *in utero* at this period have been prematurely delivered, or have shown postnatal growth disturbances or death within the first year. Werner reported three such retarded children, and four that died during the first year. The second child we reported was born of a mother who was irradiated very thoroughly late in pregnancy, was apparently normal at birth, but died when ten weeks old.

The severity of the treatment, as well as the period in development when the irradiation was given, no doubt determines the reaction of the fetal tissues. Our third case was treated during the fifth month of pregnancy, and then only locally, an effect largely due to beta-ray radiation within the vulval tumor. At the eighth month the mother was treated over the vulva with gamma-ray radiation which was equivalent to 50 per cent of the skin dose. The treatment was not severe, the fetus was not directly irradiated, and the child was apparently normal at birth and has remained so to the present time.

The second division of this study relates to the irradiation of women before conception where complete sterility is not produced. The experimental evidence in the lower animals shows with great probability

## RADIUM

that irradiation injures the follicular elements of the ovary. The first patient we reported was suffering from Hodgkin's disease and ten months before conception was heavily radiated with x-rays. A male infant was born with an extensive developmental arrest in the formation of the head and died after a few hours. The second patient was irradiated for a fibroid with gamma-ray radiation both from within and outside the uterus, and she became pregnant eighteen months later. In this instance a large, stillborn infant was born at term. Our last case was also irradiated with a gamma-ray radiation from a platinum tube placed in the uterus. Conception occurred seven months later, and the child was apparently normal at birth. Our own evidence is not sufficient to warrant our attributing the developmental defect in the first case, or the stillbirth in the second as due to irradiation.

Archangelsky irradiated with x-rays ten women suffering from tuberculosis with the intent of producing abortion and was successful in seven instances. This evidence is apparently conclusive that irradiation during early pregnancy may produce death and abortion of the fetus. The abortions reported by other clinicians and mentioned above, can hardly be considered as additional evidence because we do not know in these cases the condition of the uterine wall or other pathologic conditions.

### CONCLUSIONS

1. It is questionable whether radium or x-ray irradiation should be used to destroy the ripe follicles, leaving the immature ones injured but capable of development. This statement is made entirely on the strength of the experimental work on the lower animals and we do not feel justified in considering any of the available clinical records as adding conclusive evidence in this regard. In the treatment of menorrhagia in the child-bearing period we believe that complete sterility is preferable to the possibility of a damaged germ plasm.

2. Irradiation of the ovum during early pregnancy should never be permitted. Radiation in late pregnancy, while it may not produce gross abnormalities at birth, may hinder the growth and development of the child in later life.

### BIBLIOGRAPHY

- (1) *Beclere, M.*: Am. Jour. Roent., 1922, ix, No. 12, p. 797. (2) *Bohn, B.*: Compt. rend. Soc. de biol., 1903, xi, 1442. (3) *Perthes, G.*: Deutsch. Med. Wchnschr., 1904, xxx, 632. (4) *Hertwig, P.*: Arch. f. mikr. Anat., 1911, lxxvii, No. 2, p. 301. (5) *Hertwig, O.*: Arch. f. mikr. Anat., 1911, lxxvii, No. 2, p. 1. (6) *Hertwig, G.*: Arch. f. mikr. Anat., 1911, lxxvii, No. 2, p. 165. (7) *Schaper, A.*: Deutsch. Med. Wchnschr., 1904, xxx, 1434. (8) *Tur, J.*: Compt. rend. Soc. de biol., 1911, lxx, 679. (9) *Bagg, H. J.*: Am. Jour. of Anat., 1922, xxx, No. 1, p. 133. (10) *Perthes, G.*: Deutsch. Med. Wchnschr., 1904, xxx. (11) *Bordier*: Le Radium, 1905, ii, 410. (12) *Hastings, Beckston and Wadd*: Archiv. Middlesex Hospital, eleventh cancer report, 1912. (13) *Mavor, J. W.*: Anat. Rec., 1923, xxiv, 415, also 1922, xxiii, 99. (14) *Gilman and Baetjer*: Am. Jour. Physiol. 1904, x, 222. (15) *Baldwin, W. M.*: Anat. Rec., 1919, xvii, No. 3, p. 135. (16) *Hippel and Pagenstecher*: München Med. Wchnschr., 1907, liv, 452 and 1385. (17) *Regaud, Nogier, and Lacassagne*: Arch. D'elect. Med., 1912, xxi, 321. (18) *Cohn*: Verhandl. d. deutsch., Rönt. Gesellsch., v. 70. (19) *Leng-*



*fellner*: München med. Wchnschr., 1906, xlv, 2147. (20) *Krukenberg*: Verhandl. d. deutsch. Rönt. Gesellsch., 1909, v, 70. (21) *Walter, Fortshr. A.*: d. Geb. der Rönt., 1912, xix, 123. (22) *Hansen, F. B.*: Anat. Rec., 1923, xxiv, 415. (23) *Little and Bagg*: Anat. Rec., 1923, xxiv, 413. (24) *Lacassagne and Coutard*: Gynecol. et Obstet., 1923, vii, 1. (25) *Corscaden, J. A.*: Am. Jour. of Roent., 1922, ix, No. 12, p. 812. (26) *Steiger*: Schweiz. med. Wchnschr., 1921. (27) *Field, C. E.*: Am. Jour. of Roent., 1922, ix, 657. (28) *Polak, J. O.*: Med. Record, 1922, ci, No. 12, 493. (29) *Maury, J. M.*: Jour. Am. Med. Assn., 1920, lxxiv, 1711. (30) *Horner, D. A.*: Surg. Gynec. and Obstet., 1922, xxxv, No. 1, 67. (31) *Clark, J. G. and Black, F. B.*: Am. Jour. of Med. Sci., 1922, p. 614. (32) *Clark, J. G. and Keene, F. E.*: Jour. Am. Med. Assn., 1922, lxxix, No. 7, p. 546. (33) *Archangelsky, B. A.*: Arch. für Gynäk., 1923, cxviii, 1. (34) *Stacy, L. J.*: Am. Jour. of Roent., 1922, ix, 658. (35) *Berkley*: Jour. of Obstet. and Gynec. of the Brit. Empire, 1922, xxviii, 538. (36) *Stettner, E.*: Jahrbuch für Kinderh., 1921, xcv, 43. (37) *Aschenheim, E.*: Arch. für Kinderh., 1920, lxviii, 131. (38) *Werner*: München. Med. Wchnschr., 1921.

## A SKIN CANCER FOLLOWING EXPOSURE TO RADIUM\*

WARD J. MACNEAL, PH.D., M.D. and GEORGE S. WILLIS, M.D.,

New York

The patient, G. S. W.,<sup>1</sup> who was born, Oct. 12, 1876, had attained the age of 46 years in 1922. His father, a physician, died in 1818 at the age of 64, from prostatic hypertrophy complicated by a mitral regurgitation and nephritis. His mother died in 1918 at the age of 70 years, from angina pectoris. The patient is married and has one daughter, aged 21.

The patient has practiced medicine since 1899, and he first began working with roentgen rays in 1905, employing a Wagner static machine with attachment for fluoroscopy. He habitually used his left hand as a test object. In 1909 he became acquainted with Dr. Walter Dodd, and for several summers he worked with Dr. Dodd in the Massachusetts General Hospital. He was, therefore, fully cognizant of the danger of roentgen-ray burns because of Dr. Dodd's experience, the latter having undergone no less than forty-six surgical operations before he eventually succumbed to the sequelae of roentgen-ray burns. During 1911 and 1912 he used roentgen rays daily with the fluoroscope for examination of the stomach. In this work the palms of the hands were exposed to the rays, but always with lead glove protection. Roentgen-ray work was continued on a small scale up to 1915, and since 1917 the patient has not employed roentgen rays at all.

\*Reprinted by permission from the Journal of the American Medical Association, lxxx, 466-469, Feb. 17, 1923. Read before the New York Pathological Society, Jan. 10, 1923.

\*From the Department of Pathology and Bacteriology and the Radium Division of the Department of Surgery, New York Post-Graduate Medical School and Hospital.

1. Dr. George S. Willis, one of the authors of this report.

## RADIUM

His radium work began in 1912 with the use of radioactive water. In 1913 and 1914 he began to handle radium bromid, radium sulphate and mesothorium in glass tubes, having at his disposal about 50 mg. in all. These preparations were handled daily and very freely without protection. In 1915, much larger amounts were obtained, and he employed about 200 mg. daily, sometimes more. He habitually picked up the glass tubes to place them in metal boxes before applying the radium to the patient. In January, 1919, he obtained 365 mg. of radium in one glass tube. This he handled personally with but little precaution, from three to five times a day, in addition to smaller units in other tubes. The tubes were seized between the thumb and finger tips. This personal handling of the radium continued until 1920. Since June, 1920, he has handled radium very little, and then only with forceps. He is right handed.



Fig. 1.—Section of the first specimen, removed Oct. 28, 1922: irregular whorls of squamous epithelium, largely necrotic; marked inflammatory infiltration.

The patient observed a curious numbness in the ends of all his fingers late in the year 1918, while continuing his radium work in the army. Along with this he noted a weakness of the left arm, so that he was compelled to give up boxing, a favorite exercise. Sometimes he could not even lift a drinking glass with his left hand. This numbness has persisted up to the present time. In July, 1919, he was discharged from the Army Medical Corps and came to the New York Post-Graduate Medical School and Hospital, where he has continued his radium work. At about this time an acquaintance called his attention to the roughness of his hands, to which he had previously paid very little attention. In the following winter, about January, 1920, more serious troubles began, and ever since the hands have been a constant care. The skin became tender and sore. There was a burning sensation, sometimes an ache and often



a neuralgic pain. The skin has remained rough and harsh, and fissures have been almost constantly present. Bathing the hands in hot soda solution, nightly dressing with oil and occasional treatment by exposure to the sun's rays have been a regular part of his life since early in 1920.

About April 1, 1921, two very troublesome fissures appeared, one on the left thumb and the other on the middle finger of the left hand. At that time the hands were bathed in 5 per cent. phenol (carbolic acid) solution, and the fissures were then treated with solutions of brilliant green and gentian violet for one day. At the end of the day there was considerable redundant granulation tissue which was extremely sensitive. The next day the pain in these fissures was agonizing. Orthoform ointment was applied. At a consultation, possible malignancy was considered, but a diagnosis of infectious granuloma was made. April 10, a



Fig. 2.—Second specimen, removed November 2: portion of vascular granulation tissues containing irregular nests of atypical epithelial cells in close relation to thin-walled blood vessels; near the center, a large cell in mitosis.

culture revealed numerous hemolytic streptococci in the lesions. The patient was confined to bed for three weeks, and suffered indescribable pain. The lesions were treated by exposure to sunlight, to red light and by bathing with iodine lotion. They healed in July. After that hydrous wool fat (lanolin) was applied every night.

Early in January, 1922, daily massage treatment was begun, and was continued for about two months. Later in the month a fissure appeared through the middle of a hyperkeratosis on the ball of the right thumb. From January to June this fissure remained open continuously, and it was protected with adhesive plaster or by a bandage. Various ointments and lotions were tried. Phenol seemed to afford most relief.

In July, a fissure appeared on the middle finger of the left hand at

## RADIUM

the site of the earlier serious lesion. This was exposed to 7.5 mg. of radium in a platinum-iridium needle for twenty minutes, and it healed about August 1st. At this time he applied a similar 7.5 mg. needle of radium to the old fissure in the right thumb for twenty minutes. This was not so successful, and the fissure persisted unhealed. About August 20, this lesion suddenly became much more painful, keeping him awake at night using a bath of phenol every hour. The fissure remained the same size, but the surrounding tissue became more prominent. The patient went to the seashore, September 1, where he soaked his hands in the sea water all the forenoon and exposed them, especially the sore thumb, to direct sunlight all the afternoon. At night he put on a dressing wet

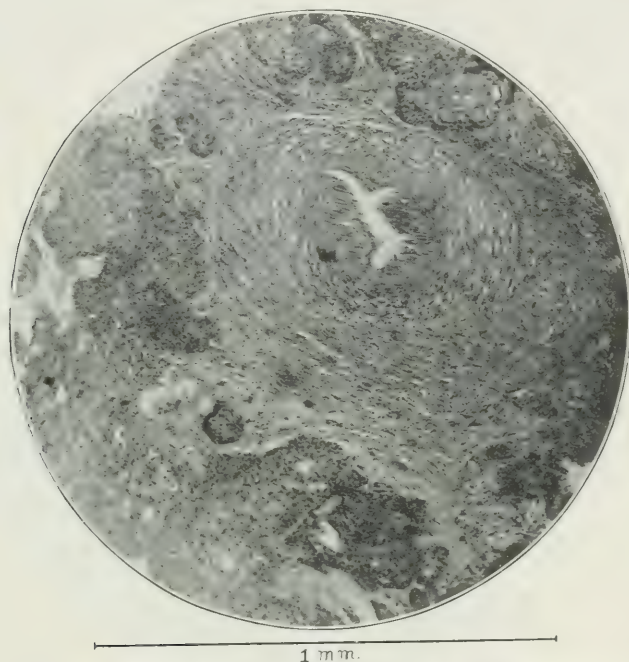


Fig. 3.—Second specimen: small artery almost surrounded by nests of tumor cells; arterial wall thickened, and the lymph spaces in the media distended; this change corresponds to the vacuolizing degeneration of Gassmann, described by him (*Fortschr. a. d. Geb. d. Röntgenstrahlen* 2: 199, 1898-1899) as a characteristic arterial lesion in roentgen-ray dermatitis; the close relation of the new growth to a vessel of this size is significant of the deep infiltration which has taken place.

with a solution of sodium hypochlorite (hyclorite), which seemed to relieve the burning. This was continued for the first two weeks of September, during which time the lesion became transformed to a flat ulcer about 10 mm. square, much larger than before and just about as painful.

September 14th, he returned to New York. A dram of scarlet red ointment mixed with an ounce of olive oil was applied for twenty-four hours. The pain at once became worse, and overproduction of granulation tissue appeared.

This treatment was stopped after one day. The pain was now so severe that the patient walked the floor every night, and was compelled to keep the hand elevated all the time.



The protrusion of granulations continued, and the lesion progressively enlarged until nearly the whole ball of the thumb was involved. Clinically, it resembled the lesions on the left thumb and middle finger of the previous year, lesions which healed. The clinical diagnosis was infectious granuloma.

Excision of the central portion of the lesion was performed by Dr. J. J. Moorhead, October 28th. The remainder of the lesion was excised, November 2nd, and the thumb was amputated by Dr. John F. Erdman and Dr. J. J. Moorhead at the carpometacarpal joint, November 4th. After the third operation there was great relief from discomfort, and the surgical wound healed with reasonable promptness.



Fig. 4.—Second specimen: skin at extreme edge of specimen; surgical incision is the left border; the carcinoma evidently infiltrates beneath the cutaneous epithelium to the surgical incision.

At present (December, 1922), the skin over the backs of the hands appears almost normal except over the distal phalanges, where the epidermis is thin, smooth, dry and translucent so that the color is red. The palmar skin of all fingers is markedly altered, rough and hard, and harsh to the touch. On the left hand this alteration extends over the palm back to the wrist. On the right hand the palm is distinctly softer. There is a thick keratosis under the nail of the left thumb, with a healed fissure running through it, and a thick keratosis along the thumb side of the left middle finger. All the nails show exaggerated longitudinal striping, more marked on the left hand.

# RADIUM

## PATHOLOGIC REPORTS.

*First Specimen.*—This tissue, removed, Oct. 28, 1922, was designated by the surgeon as "ball of right thumb, chronic inflammation of repeated radium irritation."

Gross: One piece measured 22 by 10 by 3 mm. It was mottled yellow, white and gray on one surface, and appeared to be largely necrotic. The tissue beneath was white and firmer than the surface, and showed hemorrhagic and gray markings.

The second piece measured 12 by 10 by 3 mm. This resembled the deeper parts of the first piece. It was generally soft.

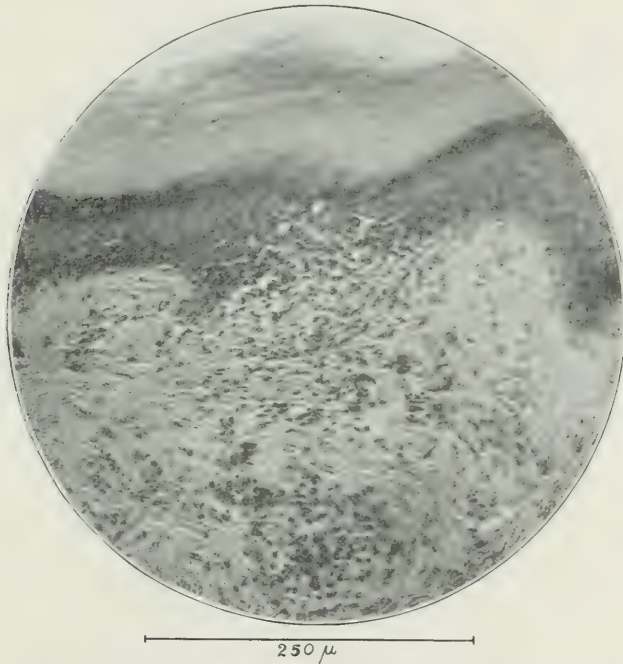


Fig. 5.—Third specimen, removed November 4; from edge of amputation incision at base of thumb; there is general hyperkeratosis, and near the center an edematous area infiltrated with round cells and plasma cells; this area includes the malpighian layer of the epidermis and the underlying dermis; it bears a suggestive resemblance to similar lesions described and figured by Unna in chronic roentgen-ray dermatitis.

Microscopic: Sections revealed the tissue to be necrotic for the most part. In it, however, one could recognize numerous irregular whorls of squamous epithelium. One small bit of tissue, which was viable, was made up of squamous epithelium with atypical cornification. In some places mitotic division figures were moderately numerous, as many as four being found in one oil-immersion field. The specimen did not present any normal tissue, so that the relationship between the normal and the abnormal could not be seen.

The appearance was highly suggestive of disintegrating squamous-cell carcinoma, but one would not be justified in making such a diagnosis without a more satisfactory specimen. It was suggested that a section



including the border of the lesion, together with some of the adjacent more normal tissue, be submitted for microscopic examination.

Diagnosis: This was: Inflamed and necrotic papilloma, suggestive of squamous-cell carcinoma. (Specimen unsatisfactory.)

*Second Specimen.*—This, removed, November 2nd, included the entire visible lesion and a margin of surrounding tissue.

Gross: The specimen measured 25 by 18 by 12 mm. It presented a gray, mottled, necrotic surface with underlying soft parts. The superficial portion appeared to be more dense than the deeper part.

Microscopic: Sections from various portions of the specimen showed extensive necrosis and infiltration with pus. Everywhere the

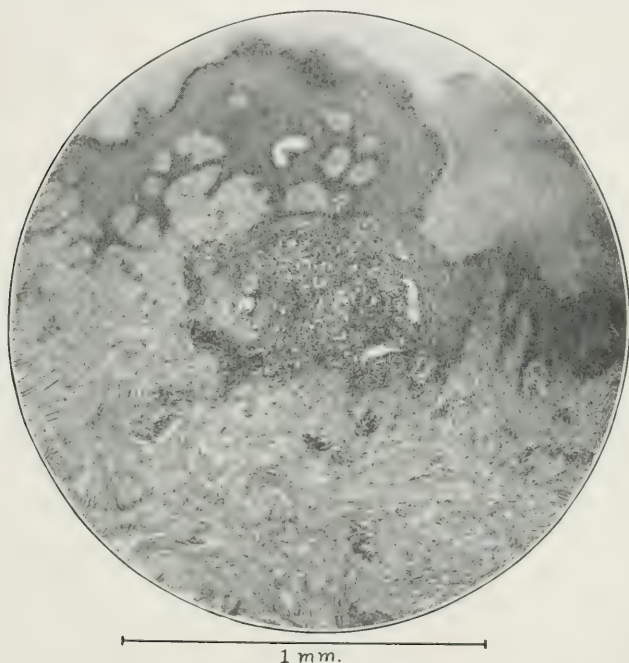


Fig. 6.—Third specimen: from the vicinity of amputation incision; the changes are of a more severe grade than shown in the preceding picture; hyperkeratosis and parakeratosis of the epithelium and exaggeration of the interpapillary epithelial ledges are distinct; near the center is a large edematous area, infiltrated with round cells and plasma cells, and involving the malpighian layer as well as the dermis; such a picture explains in part the roughness and harsh texture of the skin, and suggests a possible point for initiation of malignant activity.

connective tissue stroma was invaded by irregular nests and columns of squamous epithelial cells, many of which showed cornified centers. Groups of these cells were found infiltrating the lymph spaces close to the large blood vessels. Mitotic division figures were present in moderate numbers, and in some places as many as four could be found in an oil-immersion field. The epithelial new growth extended to the limit of the specimen in all the sections examined.

The extensive necrosis and the great irregularity in form, size and staining qualities of the epithelial cells, as well as their arrangement, all indicated a malignant activity.

## RADIUM

Diagnosis: This was: Disintegrating squamous-cell carcinoma extending beyond the limits of the specimen submitted.

On microscopic examination of the sections from this specimen, Dr. James Ewing was consulted, and immediate amputation of the thumb was advised, November 3rd. This amputation was performed early on the following day.

*Third Specimen.*—This was the thumb of the right hand, amputated at the metacarpocarpal joint.

Gross: The ball of the thumb had been cut away over an area of 37 by 23 mm. In the distal portion, under the nail, the surface was mottled gray and dark brown, and was evidently extensively necrotic.

Microscopic: Sections from the floor of the wound cavity and from

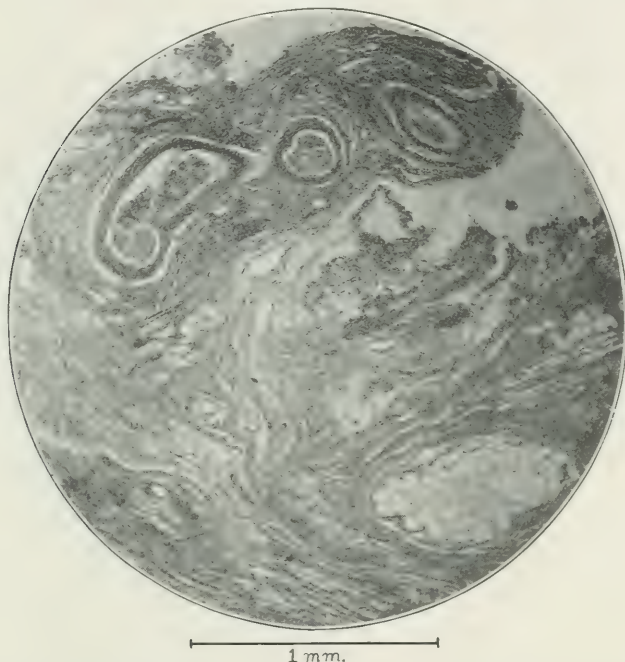


Fig. 7.—Third specimen: in upper part, sections of nerve; the fibrous sheaths are thickened; the changes have not yet been studied in detail, but it appears possible that the numbness of the skin may be related to such alterations in the nerves.

various places at its margin showed general inflammatory infiltration, and in several places small groups of the atypical squamous cells of the new growth.

Sections from the skin margin of the amputation wound disclosed that the skin was free from recognizable tumor cells. Even here, however, there was a definite excess of round cells in the lymphatic spaces about the subcutaneous blood vessels. There was also marked hyperkeratosis and parakeratosis of the epithelium.

Diagnosis: This was: Squamous-cell carcinoma of the distal phalanx of the right thumb, extending to the base of this phalanx. Mild inflammatory reaction at the site of the amputation incision at the level of the base of the first phalanx. Hyperkeratosis and parakeratosis of the cutaneous epithelium, even at the edge of the amputation incision.



## COMMENT

It will be noted that the skin at a distance from the malignant lesion showed peculiar changes which bear a remarkable resemblance to some of those that have been described by Unna<sup>2</sup> in roentgen-ray dermatitis. The detailed consideration of these changes is beyond the intended scope of the present communication. We believe, however, that they are, in this case, related to radium exposure rather than to exposure to roentgen rays.

The accompanying illustrations are sufficiently explained by their legends. They are photomicrographs, not retouched.

We are willing to admit that the earlier work with roentgen rays throws some doubt on the causal relation of the radium to the lesions in this case. On the other hand, it is also evident that the exposure to roentgen rays was slight and somewhat remote in time in comparison with the more recent intensive exposure to large amounts of radium rays. It is at least clear that this exposure to radium has not sufficed to prevent the development of the carcinoma even if we would deny it any part in the causation. We are strongly inclined to the opinion that radium may, when exposure has been sufficient, give rise to changes in the skin predisposing to development of malignant new growth, much in the same way as roentgen rays are now generally known to do, and that radium has had precisely this effect in the instance before us. The reputation for harmlessness in this respect enjoyed by radium may after all depend on the fact that, so far, not very many persons have been exposed to large amounts of radium by daily handling over long periods. With the use of larger quantities of radium there is good reason to fear that neglect of precautions may result in serious injury to the radium workers themselves. For this reason the present case report has been presented.

## SUMMARY

1. The patient worked with roentgen rays in his practice from 1905 to 1917 but not since then. Precautions for self-protection were carefully employed.

2. From 1912 to June, 1920, he handled radium, without precautions for self-protection, in small amounts up to 1915, but in quite large amounts from 1915 to 1920, from 200 to 365 mg. in individual tubes, taken between the right thumb and forefinger almost every day.

3. Various changes, which may be ascribed to the exposure to radium, began to be observed late in 1918, and since early in 1920 the skin changes have required constant care.

4. In September, 1922, a fissure on the ball of the right thumb manifested a peculiar and extremely painful alteration in character, and on excision in October this lesion proved to be a squamous-cell carcinoma.

---

2. Unna, P. G.: Die chronische Roentgendermatitis der Radiologen, Fortschr. a. d. Geb. d. Röntgenstrahlen 8: 67-91, 1904-1905.

**RESULTS OF RADIUM IN GYNECOLOGY\***

BY ALICE F. MAXWELL, M.D., San Francisco

From the Department of Obstetrics and Gynecology, University of California Medical School

Since the advent of radioactivity into the field of therapeutics, a tremendous amount of literature has accumulated on the subject. In the beginning, just as with most innovations, it was accepted almost universally by the medical profession as a panacea for the cure of neoplastic diseases. This impression, unfortunately, has been strengthened in the minds of the laymen by the publicity gained through magazine and newspaper articles. The inevitable adjustment is at hand, however, and the pendulum is now swinging towards a more conservative and sane evaluation. From the chaotic mass of individual case reports, the field of application of radioactivity is being definitely outlined and clearly defined. We offer the results obtained by radium in the Department of Gynecology at the University of California, with the hope that our contribution may aid in this process of crystallization and serve to place the subject on a more rational basis.

The material for the study consists of 162 cases which have applied to and which have been treated by our Woman's Clinic during the years 1916 to 1921, inclusive. The malignant cases comprise carcinoma of the cervix, uterine body, ovary, clitoris, and urethra. The non-malignant cases include fibromyoma and myomatous polyps and endocervicitis. We also used radium for the control of hemorrhages occurring in the adolescent and premenopausal period not occasioned by tumor growth. Once it was employed to induce the menopause in a woman who developed a psychosis with the onset of each menstrual period. A single case of chorioepithelioma was treated with interesting and instructive results. In addition to this series, we have employed radium in a few instances for the treatment of malignant conditions of the rectum and groin. The results in this group of cases have not been included in our review, since we are concerned in this study only with a purely gynecologic discussion.

*Carcinoma of the Cervix*—The relative frequency of cancer of the cervix and that of the uterine body is usually stated to be as 20 is to 1. This ratio is not confirmed by our study for, during five years, 108 with cervical carcinoma and ten with fundal growths applied for treatment. The ages of these cases ranged from twenty-eight to seventy years. Emphasis is usually laid upon the tendency of the cervical carcinoma to develop in women near the menopause, yet it must not be overlooked that the growth may make its appearance at a much earlier period. While the majority of our women were in the fourth or fifth decade, four women under thirty (3.7 per cent of the total) were suffering from advanced growths when first seen. In this connection, Wertheim, in reviewing his first series of five hundred cases, found that 66 per cent of the cancers of the cervix occurred in women under thirty years. Twenty-seven per cent (twenty-nine cases) of our women were nullipara, an interesting observation in view of the importance attached usually to the

\*Reprinted by permission from the California State Journal of Medicine, xxi, 155-158, April, 1923. Read before the Section of Obstetrics and Gynecology of the Medical Society of California, at Yosemite National Park, May 17, 1922.

trauma of child birth and to chronic endocervicitis as etiological factors of uterine carcinoma.

It is impossible in a review of this kind to give all the details of the treatment. Briefly stated, our plan has been to use the radium as a salt or emanation in a glass capsule screened by 1 mm. of brass and 1 mm. of silver. The capsule, encased in sterile black rubber tubes, has been inserted into the cervical canal and uterine body to permit as wide an area for raying as is possible. Instrumental dilation of the cervical canal has usually been avoided for fear of distributing the cancer cells. Additional cross-fire has been obtained by capsules placed in the lower uterine cavity and in the vagina in direct contact with the cervix and parametrium. We have tried bare tubes with small doses and have found them of little use save in vaginal metastasis. Many of our women presented with large sloughing ulcers which we formerly treated by actual cauterization; recently, however, we have abandoned this procedure, realizing that the exuberance of the growth could be utilized as a screen and thus permit of more extensive treatment. Gauze strips and rubber dam have been firmly packed into the vagina, to separate its walls and to protect the rectum and bladder which are emptied by enema and frequent catheterization.

The average doses have ranged from 3000 to 5000 mc. hours given either in a single treatment, or, more frequently, by the fractional method, by which a relatively large dose (2000 mc. hours) has been given at the first application and has been repeated after an interval of forty-eight to seventy-two hours. Although comparatively large amounts of the emanation are available, we have usually employed a capsule containing 100 to 150 mc. Additional treatment was occasionally given three to four months later if the symptoms returned and the visible growth had not been checked.

While we are aware of the variations in the histology and the morphology of cervical carcinoma, it has not often been possible to utilize these classifications to group our cases. The vast majority of our patients when first seen presented a stage in which the growth had lost its distinguishing characteristics. Usually, there was only a sloughing ulcer. Moreover, the fact that tumors presenting identical histologic and morphologic features may vary considerably in their clinical manifestations, rate of growth and degree of malignancy adds inevitably to the difficulty of drawing conclusions as to the response of the neoplasm to treatment.

We have divided our material into early or operable cases, borderline and inoperable growths. This division has been based upon : (1) the duration of symptoms; (2) the fixation of the growth and infiltration of the pelvic connective tissues; (3) the presence of metastatic deposits; (4) constitutional reaction. The first factor is dependent largely upon the intelligence and observation of the woman; the second is influenced by the presence of an infected ulcer with its attendant inflammatory reaction and thickening and fixation of the parametrium. This classification, however, has served as a suitable working basis.

There were 108 women with cervical carcinoma, twenty-three of whom had recurrent growths after some type of hysterectomy or cervical amputation; eighty-five had primary cervical growths. Eighty-two of this latter group received only radium treatment. Three were subsequently operated.

*Inoperable Growths (Forty-two Cases)*—Over half (51 per cent) of these patients had inoperable growths; many were almost moribund



## RADIUM

from profuse hemorrhage and cachexia; all showed massive pelvic involvement. We refused no patient in our earlier series, although we appreciated the fact that radium was useless and possibly harmful in some instances. More recently we have refused to treat the moribund cases or the very extensive cases complicated by vaginal fistulae. The fate of two of the forty-two women with advanced growths could not be determined. Thirty women (71 per cent) are dead, the majority (60 per cent) having succumbed within a few months to a year after radiation. Yet four of them lived over a period of two to three years with marked improvement of their general condition, control of the pain, and checking of hemorrhage. One of these cases merits further discussion. This woman of forty-two had a large inoperable fungating cervical mass, which was so altered by radiotherapy that the condition was considered operable. Two months after her last treatment, an attempt was made to remove the growth, but at operation it was found that the involvement was so extensive that a radical removal was impossible. The operation consisted of a simple panhysterectomy; yet this patient is entirely free from evidence of carcinoma nearly four years after operation. This possible cure must be attributed to the radium; she received intensive post-operative raying also. Two women had survived at the time of our report, although none appeared as if they would become five-year cures. Three have been followed over three years. While this group is small, we must admit that radium has had a remarkable palliative effect when 10 per cent of the cases in the terminal stage of the disease have survived over a period of three years and living has been made bearable and comfortable. We wish to lay emphasis on the point that radium helps this class of case, chiefly by cleaning up the ulcer.

*Borderline Cases*—In the borderline group were thirty-one patients (38 per cent of the series) who gave symptoms of six months to a year's duration. Ulceration of the cervix was present in all. Our records on twenty-four of these women show that over 50 per cent (thirty-one) were alive, some as long as two years after treatment. Three women were so improved as the result of raying that they were subsequently operated.

It is with this type of case that radium has been definitely more satisfactory than has surgery. While surgery rarely cures more than 10 per cent to 15 per cent of the borderline cases, Bumm has reported a 21 per cent five-year cure by radium in a series of twenty-two cases. We realize the necessity of estimating a cure by radium on a basis identical with that set up by surgical standards; namely, a five-year period of freedom from recurrence. Therefore, we draw no conclusions from our series, but feel that our results from radiotherapy with this type of case have been encouraging.

*Operable Cases*—There were only two patients with very early cases of cervical carcinoma in whom surgery was definitely contra-indicated because of cardiac complications. One woman died with an embolus one year following treatment, without gross evidence of cancer. There was no autopsy, so we do not know the actual condition. The other patient shows no evidence of carcinoma after three years. We attempt no conclusions from these cases, and believe that at present operable cases should be treated by radical surgery since the work of Bumm shows that, judged on the basis of five-year cures, surgery in early growths gives better results than radium.

*Recurrent Carcinoma*—Recurrent growths have responded less satisfactorily than any other group, possibly because the great majority of

these are not recurrences but represent the proliferation of cancerous tissues not removed at time of operation. Fifteen cases (65 per cent) of these twenty-three patients have died, usually within a year following the treatment. One of the five women who are living is clinically well after three and a half years, a result which may be due to a variation in the malignancy of the neoplasm. Three women have been lost from our records.

*Radiation After Operation*—Radium has been used prophylactically following radical hysterectomy as popularized by Wertheim. Two of the five women so treated are well after five and six years' observation, respectively. The time interval is too short with the remainder to draw any conclusions. Nor do we claim that radium plus operation was the decisive combination in these two cases. The removal was most extensive in each case.

*Carcinoma of the Uterine Body*—We coincide with the opinion that these growths are best treated by surgery, and operate all cases. We have had ten cases with fundal carcinoma. Five are dead (all advanced recurrent growths). Five are living, three as long as four years. All had been operated before radiation. Twice, while doing a panhysterectomy for fundal carcinoma, the uterus was so friable from cancerous invasion that, despite the utmost gentleness, the wall was torn through, with liberation of the neoplasm. Both women received large doses of radium post-operatively and have been followed for four years. One has recurrences.

*Carcinoma of the Ovary*—We have treated carcinoma of the ovary in six cases, one of the urethra and two of the clitoris, without good results and without apparent control of the cancer. The results of operation, however, are also extremely poor.

*Menorrhagia and Metrorrhagia*—The hemorrhages associated with adolescence, or the fibrosis uteri of the menopause, can be effectively controlled by radium. By grading the doses according to the age of the patient, we have found that the amount of blood lost at a period can be regulated practically at will. Of the fifteen women treated, fourteen were definitely relieved. One came subsequently to operation because of abdominal pain.

*Myomata and Fibroid Polyps*—Seven women were subjected to radiotherapy for bleeding from fibroids after malignancy was excluded by curettage. One patient with a fibroid reaching to the umbilicus developed a pelvic peritonitis following radiation. One with a submucous polyp continued to bleed and was subsequently operated. The others were helped. We now restrict the treatment to growths confined to the pelvis in women near the menopause, and in whom submucous polypoid tumors, malignancy or inflammatory pelvic reaction can be excluded.

*Endocervicitis*—The leucorrhea from endocervicitis was improved in all cases (four) which were selected for this type of treatment. The radium was applied intracervically. The question as to whether this treatment causes sterility is as yet unanswered.

*Chorioepithelioma*—We have treated one case by radium. A woman of fifty-three, para xv, in whom a choriocarcinoma developed fifteen years after a final pregnancy received 3420 mc. hours of radium on one application in the uterine canal. It did not arrest the growth or control symptoms and, two months later, a hysterectomy was done because of the recurrence of the uterine hemorrhage. The case is of interest in that radium is so often urged for this type of case on the ground that it readily kills embryonic cells. It had little or no effect in this case.

## SUMMARY

From our review, we feel warranted in concluding that radiotherapy has a definite place in gynecologic therapeutics. We do not believe that it cures inoperable growths, but feel that it aids the patient by cleaning up the ulcer and arresting hemorrhage. This it does in the majority of cases. Death is usually postponed and a large proportion of the cases are temporarily relieved of pain. Even more can be expected in borderline cases. Operable cases should be treated surgically after preliminary radiation. We agree that cancer of the uterine body is best treated by surgery. The bleeding of myomata in properly selected cases, the various metropathies and some of the leucorrhœal discharges can be satisfactorily controlled by raying.

## DISCUSSION

Roland Skeel, Los Angeles—I have had a little experience with radium but not enough to warrant discussion. The thing that struck me most forcibly in the paper was the fact that twenty-seven per cent of the cases of cervical cancer were nulliparous. I have never seen carcinoma of the cervix in the nullipara.

Wm. Henry Gilbert, Los Angeles—Dr. Skeel said that he has never seen carcinoma of the cervix in the nullipara, I have! It was a fatal case and one on which a Wertheim operation was followed by a recurrence treated afterwards with radium without good results. I want to compliment Dr. Maxwell on her paper because I consider it of very great importance. Personally, I have gotten to the point where I don't operate on cancer of the cervix any more. I refer them all to my radiological friends and I believe that radium, compared to the experience that I have had, with surgery and the use of Dr. Percy's cautery, is to be preferred. When it comes to cancer of the fundus, I believe that surgery is the method of preference followed afterwards by either radium or deep penetration from the high potency machine. I think that radiation is still in its infancy and we may expect much from it which will open great avenues of hope for these patients.

Frank R. Girard, San Francisco—This is indeed a question that is still in its infancy and I think it will be many years before it is thoroughly decided. Some men are taking the stand now that carcinoma of the cervix and uterus is never a surgical disease, but should always be treated by x-ray or radium. I can not bring myself to take this radical stand. There is always the advanced case, as Dr. Maxwell brought out in the paper, which we are powerless to treat by surgery and which can be made comfortable for the remainder of life by radiation. Carcinoma of the body of the uterus is undoubtedly primarily a surgical disease to be followed by radium later. I think the very early cases of cervical cancer which we occasionally see and which I hope we may see oftener, as people become educated to the importance of consulting their physicians on the appearance of early symptoms, will be followed by a larger proportion of cures if the radical operation is combined with radiation. I would feel safer treating these cases by surgical methods plus radiation rather than by radiation alone.

James Percy, San Diego—There are so many sides to this question that I have been lying dormant in reference to the cautery. I have been watching my cases and I am interested in the statement that was made in the paper about cauterization having been abandoned. The



cautery has never been mentioned in the literature more frequently than at the present time. You can't down the cautery in cancer. It is the only thing that survived with the human race and is still the most certain treatment for cancer that we have. The only thing is that we think of the cautery as a red-hot, white-heat instrument of torture. That day will soon be gone. There is nothing that the cancer cell succumbs to so quickly as heat. Just 113 degrees Fahrenheit for ten minutes and you cannot transplant any cancer cells. Now it is a mere question of dissemination. It is curious to me that gynecologists have forgotten the work of John Byrne who deplored the use of the knife.

Jones, Long Beach—With regard to the surgery, Dr. Crile says, "Handle the tissues lovingly," and I am very much afraid at times that we do not get results from surgery sometimes because we do not handle the tissues lovingly enough. Personally, I have used, in the last six or seven years, radium following surgery in quite a number of the so-called non-operable cases. I do believe that if we will be more careful in handling our carcinomatous tissue we will not have as many recurrences.

Margaret Schulze, San Francisco—We believe that our results have been a good deal better with the radium than with the cautery. The comparatively good results in the borderline type of case tends to make us consider operating upon a patient very much more seriously than we might have at an earlier time when we did not have the radium. The borderline case does a great deal better with radium than with operation and so we want to make sure that it is not a very early operable case before we subject the patient to radium. Inoperable cases are much better treated by radium alone.

---

## NOTES ON THE CLINICAL VALUE OF RADIUM IN THE MANAGEMENT OF UTERINE HEMORRHAGE\*

### SOME END RESULTS.

By JOHN OSBORN POLAK, M.Sc., M.D., F.A.C.S., Brooklyn, N. Y.

(From the Clinic of the Long Island College Hospital.)

RADIUM has established for itself a definite place in gynecology in the treatment of uterine hemorrhage; not only in the bleeding caused by fibroids, but in the so-called myopathic bleeding in young girls and spinsters, and the excessive menstrual flow met with in women with subinvolution and fibrosis of the uterus. It has a further place in the treatment of leucorrhea resulting from cervical inflammation, and while it cures this condition by the destruction of the glands and the substitution of scar tissue, it is less destructive to the cervical tissues than any of the several forms of excision.

Its admitted use in cancer is granted, and personally we feel that it is only a matter of time when it will replace operation, for all cancer is cured by the individual producing an immunity against the disease. This immunity, operation breaks down, and hence cancer grows and metastasis takes place unless the removal has been complete. Gaylord has shown that it is possible for mice and rats to produce immunity against im-

\*Reprinted by permission from the Medical Record, ci, 493-4, March 25, 1922.

## RADIUM

planted growths and live for months and even years with a localized swelling which has no tendency to spread until the resistance is lowered by blood loss or anesthesia—then the cancer promptly grows.

When one thinks of the long, radical operation, with its extensive tissue exposure and trauma and the prolonged anesthesia necessary to perform this operation, one can readily see how the patient's immunity is necessarily reduced. This explains the prompt recurrence following many of our incomplete efforts at removal and is to me the most striking illustration of why radium, which has a special selective action for certain tumor cells, effects a cure, or at least increases the longevity, for the individual resistance is not impaired.

During the past six years we have been using radium almost daily, with more or less success. Our follow-up system, which is detailed, has given us the opportunity to see the results, modify our indications, and limit the forms of application.

First of all, let me say, that there is a decided difference in the application, as well as the results where the radium element is used and where the emanation is used; also let me say that intensive radium treatment, with one or two grams of radium element, does not enter into this discussion. Our results have been obtained, and what I have to say will apply to the man who has at his disposal from fifty to one hundred and fifty mgms. of radium element. The results which we have obtained can be had by the intelligent use of this amount.

While it is impressive to see the wonderful cures presented at the weekly conferences at the Memorial Hospital, these results have little clinical or practical bearing on the cases you and I will treat with our 100 or 150 mgms. of radium.

*Myopathic Hemorrhages in Young Girls.*—These bleedings are frequently excessive, some yield to the internal administration of endocrines and regulation of the lower bowel. When the bleeding has continued for any length of time, the endometrium becomes hypertrophied, and the uterus large and soft, and the os is very likely to be open. These cases were formerly curetted after all other forms of internal medication had failed, and a secondary anemia had been induced. After curetting there was usually an amenorrhea for a month or two, when this was followed again with a metrorrhagia. This same case treated by radium, for from 300 to 600 mgm. hours with the radium properly filtered with glass, silver, and brass, and this covered with rubber, which practically cuts out all of the alpha and beta rays, will establish a normal menstruation after one séance. Once only have we had occasion to repeat the exposure. In this class *there were 31 cases treated, the average dosage was 400 mgm. hours, and only one application was given in 30 of this series.* The results show that the quantity of the menstruation was regulated in every instance, except one, which required two subsequent applications. The last was followed by amenorrhea for one year, when the menses were reestablished and recurred regularly. Six of these girls are now married, and two have become pregnant, a fact which answers some of the criticisms which are made of using radium in young girls.

*Radium in Myomata.*—Radium will control the hemorrhage of uterine myomata and in a large number of cases will reduce the size of the tumor, provided the tumor is intramural or submucous, and not pedunculated. Nevertheless, operation is still the procedure of choice in most myomata, for the indications for radium are limited and it has certain definite *disadvantages*, such as: First: While it controls bleeding, and in

the majority of cases reduces the size of the tumor, nodules outside of the uterus may be left without a blood supply and consequently are more likely to give trouble.

Second: Malignant complications, already in the tumor, may be overlooked, for it has been shown that sarcoma is found in serial section in about 9 per cent. in submucous tumors—consequently we can lay down the dictum that radium is never permissible in submucous growths or unless a diagnostic curettage is possible, for while remarkable results have been shown following radiation of cervical cancer, body carcinoma is not amenable to the effects of the rays.

Third: About 54 per cent. of all fibroids are complicated by some form of tuboovarian disease, consequently many of these intrapelvic complicating lesions are missed, and while the tumor is shrunk, and the hemorrhage controlled the associated lesions help to keep up the patient's invalidism.

Fourth: Radiation, when applied in sufficient dosage to check hemorrhage and shrink the tumor, will seriously impair the reproductive functions in young women, and therefore should not be used as a procedure of choice in this class of cases.

Fifth: One of the symptoms of fibroid which requires treatment is the pressure symptom—here the effect of radium is too slow to relieve the conditions which intraligamentous growths produce on the ureters and blood vessels.

Sixth: The immediate effect of radium is the production of edema and excitation of inflammatory reaction; hence, in the presence of old inflammatory adnexal lesions, this reaction becomes more marked.

Finally: Radiation will increase the necrosis in tumors which are already necrotic, and by added acidosis increase the toxemia of the patient.

Against these disadvantages radium has certain definite advantages in the treatment of fibroid tumors, particularly if proper selection is made. These *advantages* are: First: There is no operative mortality. There is no general anesthetic. There are no postoperative complications, and there is prompt control of uterine hemorrhage.

Second: Should radium fail, operation is always possible.

Third: The menopausal symptoms are not so marked.

Fourth: In intramural tumors we can not only expect absolute cessation of the hemorrhage, but shrinking in the tumor in over 65 per cent. of the growths.

Fifth: Radium is the procedure of choice in myomata complicated by heart disease, extreme anemia, diabetes, and chronic nephritis.

We have confined radiation in fibroids to those tumors which are not larger than a four months pregnancy, where the growth is definitely intramural, and there are no subperitoneal modules of any considerable size; and to those submucous tumors which, after careful examination under anesthesia, are shown to be sessile.

In all we have treated 106 of these growths by radiation. These patients have had from 2,000 to 3,000 mgm. hours; the radium element has been applied directly to the interior of the uterus, the alpha and beta rays have been excluded by proper filters. I have the follow-up records of all of these cases, and only two have needed subsequent operation; in these, both large submucous tumors, the bleeding recurred, and on operation it was found that the tumors had undergone a marked edema.

In 104 the bleeding ceased and has never recurred, after the first



menstruation, which was more profuse in a number of instances than some of the previous bleedings. This, in turn, was followed by a sero-sanguinous discharge, which persisted for several weeks. In 80 of these tumors the growth had shrunk to less than half of the original size, and in 20 it has entirely disappeared.

The largest class of cases which come to us for relief are the bleedings resulting from subinvolution and fibrosis of the uterus without lateral or posterior parametritis, or a history of pelvic inflammation.

My associates and I have seen and applied radiation to 260 women, who can be included in this class. There have been no failures to check the bleeding, and the majority of these uteri have, after a period of several months, become senile in character, and menopausal symptoms have appeared. Several in this class which were associated with prolapse have subsequently been operated upon, and the uterus interposed under the bladder with resulting cures of the descensus.

20 Livingston Street.

---

## CLASSIFICATION AND RELATIVE VALUE OF THE VARIOUS METHODS EMPLOYED FOR THE INTERNAL ADMINISTRATION OF RADIUM EMANATION AND RADIUM SALTS\*

By WILLIAM H. CAMERON, M. D., and CHARLES H. VIOL, Ph.D.,  
Pittsburgh, Pa.

In this communication, it is our intention to suggest a classification for the various methods of employing radium emanation and radium salts internally. We believe a working classification necessary in order that the terminology of the subject may be more generally understood, and that the relative therapeutic and economic value of the several methods advocated, may become better known by the profession at large.

Many units have been used to express concentrations of radium emanation and quantities of radium salts. This led to uncertainty and confusion when these substances were used and it was recognized that there was a great need for an international standard and a better defined unit for expressing the concentration of radium emanation. As a result of the work of the committee appointed by the Congress of Radiology and Electricity at the Brussels meeting in 1910, Madame Curie in 1911 prepared a standard which was accepted in 1912 as the International Radium Standard. A prototype standard was also prepared and is kept at Vienna in the Institute for Radium Research of the Vienna Academy of Sciences. Standards which have been carefully compared with the International Standard and the Vienna Secondary Standard are now in the possession of different countries, including the United States Bureau of Standards at Washington. At the above mentioned Congress, it was further decided to call the quantity of radium emanation which is in equilibrium with one gram of radium element—the “curie” in honor of M. and Mme. Curie. The curie is a very large unit and, for ordinary

---

\*This paper was first published in RADIUM, iv, 57-68, January, 1915. On account of renewed interest in the subject it was thought advisable to revise it for re-publication.

use, it is more convenient to express quantities of radium emanation in terms of the millicurie and microcurie, these being respectively one-thousandth and one-millionth of a curie and equal to the radium emanation in equilibrium with one milligram and one microgram of radium element. The mache unit, much used in the past in Germany and Austria to express concentrations of radium emanation, is a much smaller unit than the microcurie. One microcurie of radium emanation per liter equals a concentration of 2700 mache units.

On the basis of Rutherford and Soddy's "disintegration theory" the accumulation of radium emanation may be explained as follows: All the radioactive elements are disintegrating or transmuting at a rate that is definite and invariable for each radio-element. Thus, the time required for the disintegration of half of any quantity of radium is about 1700 years. For radium emanation the period of half decay is 3.85 days. In any given quantity of radium there are being produced every second a certain number of atoms of emanation due to disintegration of radium atoms, this number being a very small fraction (0.000,000,000,01) of the total number of radium atoms present. If the radium is initially freed from emanation atoms by any suitable means, there will be formed in the first second this same definite proportion of emanation atoms, and of these a certain proportion (0.000,002) will change in the next second into the next product, Radium A, but not all will change. In the second second, more emanation atoms are formed and since there are now these together with the emanation atoms remaining from the first second, the number of emanation atoms changing in the second second is greater, since it is always the same fraction of all the emanation atoms present (0.000,002). In this way there is a piling up of the emanation atoms until the number of these changing per second into Radium A equals the number produced per second from radium atoms. This limiting condition is called that of radioactive equilibrium. In a sealed radium preparation, this condition of radioactive equilibrium between the radium and the emanation is half attained in 3.85 days. It is approximately attained in a month. The following table shows the decay of radium emanation and the rate of accumulation of emanation in a sealed radium preparation:

A equals fraction of emanation remaining after time.

B equals fraction of equilibrium amount of emanation formed in t days in a radium preparation initially free from emanation.

Time	A	B
0	1.0000	.0000
1 hr.	.9925	.0075
6 hrs.	.9560	.0440
12 hrs.	.9139	.0861
18 hrs.	.8737	.1263
1 day	.8353	.1647
2 days	.6977	.3023
3 days	.5827	.4173
4 days	.4868	.5132
5 days	.4066	.5934
6 days	.3396	.6604
7 days	.2837	.7163
8 days	.2369	.7631
9 days	.1979	.8021
10 days	.1653	.8347
12 days	.1153	.8847

**RADIUM**

Time	A	B
14 days	.0805	.9195
16 days	.0561	.9439
18 days	.0392	.9608
20 days	.0273	.9727
25 days	.0111	.9889
30 days	.0045	.9955
40 days	.0007	.9993
50 days	.0001	.9999

Being a gas, radium emanation when present in any preparation, has a great tendency to escape, since the amount of emanation normally present in the air is an exceedingly small quantity. Some solids such as minerals and charcoal hold the emanation with considerable tenacity, but if the solid is finely divided and the air supply is sufficient, all the emanation will eventually be lost. Because of the ease with which emanation diffuses away from solutions, etc., it is always necessary to use great precautions to avoid such mechanical losses. So, for example, when a solution of radium emanation is being taken per os, it should be drunk through a tube from the original container, as the splashing and exposure incident to pouring the emanation water into a glass will cause a large loss of emanation. Again the emanation is not very soluble in water. In a closed vessel half filled with water, at ordinary temperature (20-25° C.), emanation would be so distributed that four-fifths would be in the air space and one-fifth dissolved in the water; that is, the concentration of the emanation in the water would be one-fourth the concentration of the emanation in the air above. For this reason, it is necessary to use all of any emanation preparation at one dose. If for example, a bottle of emanation water were half emptied, at a dose, in a short time four-fifths of the remaining emanation would pass into the air space above and the second dose would contain only one-fifth as much emanation as did the first dose.

The radioactive decay of emanation is such that in 3.85 days, half disintegrates, and so on, so that after a month practically all the emanation has decayed. Of course, if radium is present in the preparation the decay of the radium produces more emanation—but in any emanation preparation (such as most of the naturally active mineral waters) after one month, practically all of the emanation has disintegrated and the radioactivity of the water is almost nil.

The necessity of giving exact data in regard to the quantities of radium salt and concentrations of radium emanation employed cannot be too strongly emphasized. Unless such data (based on actual electroscopic measurement by reliable authority) are given when making the case reports, they lose value, since there is no possibility of comparing results with those of others who may or may not have worked under the same conditions. It should also be clearly stated which method has been employed.

Depending upon the radioactive substances used, there are, in internal medicine, two main divisions recognized:

First—Administration of radium emanation (Part A and B.)

Second—Administration of radium salt (Part C.)

We will take up the consideration of the various methods of administering radium emanation, the dosage employed and a short description of its properties.

Radium emanation is the disintegration product resulting after radium atoms have undergone a transmutation consisting in the emission



of an alpha particle (ray). The alpha particles are positively charged helium atoms shot out with tremendous velocity (9,000 to 12,000 miles per second) from the parent atom. Radium emanation is a gas which is absolutely inert—chemically—forming no compounds. One curie of emanation gas has a volume of 0.6 cubic millimeters at 0°C and a normal pressure of 760 mm. The weight of a curie of emanation is 0.006 milligrams. Radium emanation transforms by loss of an alpha particle, into Ra A, which in turn loses an alpha particle and produces an atom of Ra B. Ra B changes by loss of a beta particle (negative electron) into Ra C, which by loss of a beta and then an alpha particle, goes over into the slowly decaying Ra D, or radio-lead.

In order to study the various methods, the following classification based on the source of radioactivity, was adopted:

A—Naturally Occurring Emanation:

- |                 |   |   |
|-----------------|---|---|
| 1. Inhalation   | } | Room  |
| 2. Deglutition  | } | Bath  |
| 3. Hypodermatic | { | Intermuscular<br>Intra-articular<br>Intravenous |
| 4. Enema        |   |   |

B—Artificially Prepared Emanation:

- |                 |   |   |   |                              |
|-----------------|---|---|---|------------------------------|
| 1. Inhalation   | { | Room Type                                       | } | Diffused by air<br>or oxygen |
|                 | { | Individual Type                                 | } | Diffused by air<br>or oxygen |
|                 | } | Bath  |   |                              |
| 2. Deglutition  |   |   |   |                              |
| 3. Hypodermatic | { | Intermuscular<br>Intra-articular<br>Intravenous |   |                              |
| 4. Enema        |   |   |   |                              |

C.—Administration of a Soluble Radium Salt:

- |                     |   |   |
|---------------------|---|---|
| 1. Deglutition      | { | Drinking Solution<br>Tablets, Pills, etc.       |
| 2. Hypodermatic     | { | Intermuscular<br>Intra-articular<br>Intravenous |
| 3. Bathing Solution |   |   |
| 4. Enema            |   |   |

Part A.

*The Administration of Naturally Occurring Emanation—Room Inhalation.*—This method consists in placing patients in an air-tight room or compartment, into which, or through which, a stream of natural radioactive water is flowing. The concentration is influenced by the amount of emanation taken up by the water in its course through some deposit of radioactive material in the depth of the earth, and by the rate by which the emanation is given off after it reaches the room or compartment.

Because of the uncertainty in the determination of the dosage, which should be expressed in terms of microcuries per liter of air, the difficulty of adjusting it to the individual case, and on account of the inadequate concentration of most natural waters, we believe this method, used alone, is therapeutically inadequate and that cases so treated should not be considered in compiling statistics.

## RADIUM

*Administration of Naturally Occurring Emanation—Natural Radioactive Bath.*—There is considerable dispute among workers abroad as to the power of radium emanation to penetrate the skin. We believe that little, if any, absorption actually takes place and that the therapeutic effect is derived entirely from the inhalation of the emanation as it comes from the water. Such being the case, opportunity should be given the patient to inhale all the emanation possible. This can be controlled to some extent by erecting a tent over the tub. Unless the natural radioactive water used is of a suitable temperature for a more or less prolonged immersion, considerable emanation will be lost in the process of heating the water. The higher the temperature the more rapidly will the emanation be given off and this factor must be considered in working out a technique for the individual case.

The best method of determining the dose used is by an analysis of the air confined in the air space at time of treatment. An approximate dose can be determined by a knowledge of the emanation concentration of the water. The dosage should be expressed in terms of microcuries of emanation per liter of water in the tub or per liter of confined air above the water line.

If sufficient concentration (in our opinion not less than 0.05 microcuries per liter) is present in the natural water, this method may be of some value as it combines the effect of a continuous warm bath with emanation. However, what has been said as to the therapeutic value of the inhalation of naturally occurring emanation when used alone also applies to this method.

*Administration of Radium Emanation—Deglutition.*—The only practical method of getting naturally occurring radium emanation into the system is in the form of naturally occurring radioactive drinking water, this by reason of the fact that it can be taken at frequent intervals. It is unfortunate that the decay is so rapid (half period being 3.85 days) for it makes it impractical to use naturally occurring radium emanation at any great distance from the source of supply. If the water originally contained 1 microcurie, at the end of four days it will contain  $\frac{1}{2}$  microcurie; and at the end of eight days  $\frac{1}{4}$  microcurie, and at the end of thirty days practically all radioactivity will have disappeared. Hence natural radioactive waters can never be used for general distribution.

There are only a few natural springs in the world of sufficient dosage to give a true therapeutic effect and when results are obtained, except in the mildest type of cases, it is perhaps due to the continued effect which comes from frequently repeated doses. The original emanation concentration can be accurately determined by electroscopic methods and if the rate of decay is properly calculated, the dose of any single quantity can be determined at any period before consumption. The dosage should be expressed as microcuries or millicuries per liter.

*Administration of Naturally Occurring Radium Emanation—Hypodermatically.*—From a therapeutic standpoint the intermuscular, intra-articular and intravenous injection of naturally occurring radium emanation, in the form of naturally occurring radium emanation water, is practically worthless. It is difficult to properly sterilize such a solution without a great loss of the emanation; consequently the dose is inadequate.

*Administration of Naturally Occurring Radium Emanation Water—Enema.*—Because of the slight activity of most natural waters, this method of application is of no value.

## Part B

*Administration of Artificially Produced Radium Emanation—Inhalation, Room-Type.*—This method consists in conveying the emanation produced by a soluble radium salt in solution by means of an oxygen stream or compressed air into an air tight room or compartment. Oxygen is not only used to convey the emanation, but to replace oxygen in the room which has been used up by the patients in breathing. It is more economical, however, to use air under pressure for this purpose, in which some arrangement should be made for pumping the air out of the room, washing out the excess carbon dioxide and returning the air without loss of emanation.

The available dose for each patient can be estimated from the known amount of radium element in solution and the air capacity of the room. The exact dosage available can be determined by an electroscopic examination of the room air for emanation at the time of treatment.

This method has the disadvantage of confining a number of persons in a closed room, the carbon dioxide content of which is considerably above normal; the possibility of bacterial contamination; the difficulty of individual dosage; and, due to the short length of time it takes for the blood to lose the emanation after the patient has passed out of the room, the treatment can only be effective when intensive dosage is administered.

In our experimental work we used, on human beings, the emanation produced by 2 to 74 milligrams radium element, giving a room concentration of from 0.003 to 0.8 microcuries per liter of air (3 to 2100 mache units). On animals, we succeeded in securing a lethal dose by the use of a concentration of 2600 microcuries per liter of air (70,000,000 mache units).

The results obtained from low concentrations of emanation were practically nil and it is best that about 25 milligrams of radium element should be employed in this work. It was demonstrated by examination of the blood of patients for emanation, that in three hours practically all the emanation had disappeared. Therefore, treatment by this method always should be augmented by additional emanation given in the form of emanation drinking solution.

*Administration of Artificially Produced Radium Emanation—Inhalation, Individual Type.*—In this method, the emanation instead of being set free in a room is carried to an individual inhalation apparatus placed over the mouth and nose. The multiple type (for treating more than one patient at a time) has the advantage of permitting patients to sit or lounge in a well lighted and well ventilated room and an arrangement can be had which allows better regulations of dosage for the individual case. The one or two patient type can be made portable and has the advantage of being able to use a less amount of radium element to secure the same individual concentration. It can be used also in hospital work for bedfast patients, in which case the available concentration can be augmented by erecting a tent on the patient's bed.

*Administration of Artificially Produced Emanation—Inhalation, Radioactive Bath.*—This form of administration of emanation consists in rendering the bath water radioactive by taking the emanation from a soluble radium salt in solution. It has the advantage over the natural radioactive water in that it can be made any concentration desired, depending, of course, on the amount of radium element. What we have



described under the natural bath water as to estimation of dosage and technique also applies to this method.

*Administration of Artificially Produced Emanation—Deglutition.*—Many substances are capable of being rendered radioactive, but, on account of the rapid decay of the emanation, the only practical and economical method of administering is in the form of radioactive water. The method of production is simple and does not require an elaborate equipment. It consists in conveying the emanation, produced by a soluble radium salt in solution, into a container filled with distilled water. As the emanation is also soluble, the concentration in the distilled water is in direct proportion to the amount of radium contained in the soluble salt. Like the natural waters, artificially produced emanation water is not a permanently radioactive solution and, therefore, it is not a practical commercial possibility, except where it can be delivered fresh every day. It has a decided advantage over naturally occurring water, in that the concentration can be made any strength desired, and when used in sufficient dosage at frequent intervals, is the most effective single method of administering emanation products.

We have used on human beings, emanation solutions containing from 1 to 10,000 microcuries (2700 to 27,000,000 mache units), our maximum dose being by far the largest dose ever attempted. We consider a dose with an original emanation concentration of less than 1 to 2 microcuries as insufficient, and an average daily dose of radium emanation should be 10 to 20 microcuries (27,000 to 54,000 mache units). A fair dose would be from 14 to 21 microcuries. In this connection, it is well to mention the fact that the Radium Institute of London administers 250 to 500 microcuries of emanation as the daily dose (700,000 to 1,400,000 mache units).

Numerous machines have been put on the market for the production of radioactive water. The principle of these machines is the enclosing of an insoluble radium salt in an unglazed porcelain or other pervious capsule or rod, the idea being to have the emanation escape into the water in which the radium container is immersed. Considering the fact that the amount of emanation actually able to pass out would be only from two to ten per cent of the amount produced by the radium contained, we do not believe, from an economic standpoint, that this method is practical since very large amounts of radium element must be used in order to secure sufficient dosage, thus making this form of treatment almost prohibitive from the standpoint of cost.\*

*Administration of Artificially Produced Radium Emanation—Hypodermatically.*—The preparation of a solution for intra-articular, inter-muscular or intra-venous injection in this way is possible because distilled water or normal physiological salt solution can be used in the preparation of same. To secure sufficient dosage, the emanation from a large amount of radium is necessary. For practical purposes, therefore, this form of using emanation is not generally available.

*Administration of Artificially Produced Radium Emanation—Enema.*—A solution for use as an enema can be prepared as described in the preparation of emanation solutions for drinking purposes. The water cannot be redistilled or sterilized without loss of emanation. As

---

\*There are on the market devices to impregnate water with radium "emanations" (rays) which consist usually of a small amount of a radium ore in powdered form, hermetically sealed in a glass tube. This tube is to be suspended in a sealed bottle of water to "activate" the water. Needless to say, no radium emanation passes through the glass into the water, and the rays from the vanishing amount of radium, etc., produce no effect on the water that has any medicinal value. The device is a therapeutic fraud.

the emanation would not be taken up so rapidly, it would be necessary, then, to have a large concentration in order to secure a physiological effect.

## Part C.

### INTERNAL ADMINISTRATION OF RADIUM SALTS

- |                       |   |                                |
|-----------------------|---|--------------------------------|
| (a) Deglutition.      | } | Drinking Solution.             |
|                       | } | Tablets, Pills, Capsules, etc. |
| (b) Hypodermatic.     | { | Intermuscular.                 |
|                       | { | Intra-articular.               |
|                       | { | Intravenous.                   |
| (c) Bathing Solution. |   |                                |
| (d) Enema.            |   |                                |

Wickham and Degrais in their report to the Congress on Physico-Therapy conclude as follows: "Subcutaneous, intravenous, intrapulmonary, intraperitoneal, intrapleural and subarchoid injections of radium sulphate are harmless; even in infants there is, during the first two hours after injection, only a slight and transient state of cardiac depression or stimulation."

In co-operation with Doctor Frederick Proeschler and others, we have carried on extensive experiments with the use of radium element internally, using from 1 to 10 micrograms in 60 c.c. of water by mouth and from 10 micrograms to five milligrams in 2 cc. of normal physiological salt solution, given intravenously. As far as we are able to learn, this has been the most extensive work carried out in internal administration of radium. Even with the use of 5 milligram doses, we have, up to this time, never seen the slightest ill effect, the only contraindication noted being an extremely low blood pressure.

The following table shows the distribution of radium salts following an intravenous injection of one milligram radium element in the form of a soluble salt. It is to be noted that by far the largest percentage is recovered from the bone and bone marrow, where it is deposited as an insoluble salt. It is to be noted further that the carcinomatous tissue present in this particular case does not show an excessive percentage of radium.

One Milligram Radium Element Injected, September 1, 1913.

Diagnosis—Cancer of the Uterus.

Autopsy held—December 17, 1913.

No.	Part	Wet Weight gm.	Dry Weight gm.	Radium in Sample micrograms	Megm. Per Gram Dry Weight
1.	Heart tissue . . . . .	11.7	2.26	.000118	0.00005
2.	Aorta tissue abdominal . . . . .	13.4	2.27	.00219	0.00080
3.	Bone marrow (sternum) . . . . .	20.5	7.01	.04414	0.00630
4.	Liver . . . . .	11.9	2.48	.01530	0.00610
5.	Suprarenal capsule . . . . .	5.3	0.91	.000118	0.00013
6.	Carcinomatous tissue mass of the parametrium . . . . .	12.4	2.17	.000275	0.00012
7.	Parathyroid gland	0.12	0.035	Trace?	.....
8.	Bone marrow lumbar region . . . . .	9.18	3.73	.01780	0.00480

## RADIUM

No.	Part	Wet Weight gm.	Dry Weight gm.	Radium in Sample micrograms	Megm. Per Gram Dry Weight
9.	Intestines .....	17.7	5.10	.000700	0.00014
10.	Thyroid gland ....	13.3	2.74	.000700	0.00026
11.	Kidney .....	15.0	3.41	.000090	0.00003
12.	Stomach .....	15.5	3.30	Trace?	.....
13.	Lung .....	4.77	0.82	.00163	0.00200
14.	Pancreas .....	7.12	1.38	.00059	0.00043
15.	Spleen .....	11.83	2.90	.00196	0.00067
16.	Retroperitoneal gland .....	26.6	11.80	.00141	0.00013

*Internal Administration of Radium Salts—Deglutition, Drinking Solution.*—By dissolving soluble radium salts in redistilled water containing a slight amount of hydrochloric acid. The solution should contain enough radium element per dose to give a daily dose of not less than 4 micrograms of radium. As will be seen later, this is the most economical method of administering radium salts by mouth. The solution not only has the advantage over emanation water by being permanent and, therefore, practical, but it represents definite dosage and will, by reason of the retention for a greater or less period of the radium salts in the stomach and intestinal tract, give a more prolonged therapeutic effect. Standard radium solution for drinking is now supplied in the form of ampules containing 2 c.c. of solution, acidulated with hundredth normal hydrochloric acid, each ampule having 2 micrograms of radium element in the form of radium chloride in solution permanently. It must be mentioned that because of the acidity, such solution for drinking should not be used for injecting purposes.

The dosage can be accurately determined by the electroscope and should be expressed in micrograms of radium element per dose.

*Internal Administration of Radium Salts—Hypodermatically.*—The only practical method of preparing solutions for intermuscular intra-articular or intravenous injections is by the use of a soluble radium salt, for by this method permanent and absolutely sterile preparations can be obtained, and, furthermore, exactness in dosage is assured. As before stated, we experimented with dosages ranging from 5 micrograms to 5 milligrams, put up in ampules containing 2 c.c. of physiological salt solution. At the present time, we consider a single dose of from 50 to 100 micrograms as therapeutically correct and absolutely safe. This amount can be repeated every 10 days, until the patient has received 300 micrograms. A larger cumulative dose, we consider not necessary for ordinary work. Our experimental work with the intermuscular and intra-articular injection was not extensive, as our knowledge of the physio-chemical and bacteriacidal powers of radium as applied in therapeutics, urged us to place it in the blood stream by the most direct route. In other words, we felt that the maximum effect of radium administered internally was obtained when it was injected intravenously, the blood stream at once carrying the radium to all parts of the system. Standard radium solution for intravenous injection is now supplied in ampules containing 2 c.c. sterile normal salt solution with 10, 25 or 50 micrograms of radium element present in the form of a soluble chloride.

*Internal Administration of Radium Salts—Bathing Solution.*—Bathing solution must, of course, be permanent and can only be made so by the addition of soluble radium salts. Individual bath stock solutions should contain enough radium element which, when mixed with



the bath water, will give a concentration of from 1 to 10 microcuries. Strictly speaking, this form of administration is by inhalation, and is only mentioned here because soluble radium salts should be used in the preparation of the stock solutions. Where radium solutions are taken per os, or by injection the actual radium salt is brought into the system and as will be shown, is only slowly eliminated. Where a radium solution is used in the bath, only the emanation gets into the system, and this is rapidly eliminated after coming from the bath. As a matter of fact, this form of radioactive bath is the only one in which a definite dose of emanation can be satisfactorily administered. What has already been said regarding the technique of radioactive bath also applies to this method. The dose should be stated as so much radium element per liter of bath water. The temperature of the water and duration of bath should be mentioned. Mention should also be made as to the open or closed (tent erected over tub) method.

*Internal Administration of Radium Salts—Enema.*—We are not prepared to give an opinion as to the comparative therapeutic value of this method, as we consider that the accumulated emanation in the stock solutions would be entirely lost during the process of preparation for administration. The stock solution, should be put into a container that will permit heating of the fluid to at least 100 degrees F. while still under seal. The container should then be connected directly to the rectal tube. Such a method may prove of value provided that the solution contains not less than four micrograms of radium element per dose.

In conclusion, we again desire to call the attention of physicians to the necessity of stating the correct dosage and to warn them that they must be absolutely sure that they are using preparations, the emanation concentration or radium element content of which cannot be questioned. All pharmaceutical radium preparations should be viewed with distrust if the radium content of the preparation is not specifically stated and guaranteed.

## APPENDIX

"A great many experiments\* have been carried out on the effects of intravenous injections of soluble radium salts, and on the effects of radium solution per os, and it therefore was important for comparative purposes to know the relative rates of excretion of the radium when using either of these methods. The intravenous solution, most commonly used, contains 50 micrograms (0.05 mgm.) of radium element in the form of radium chloride dissolved in 2 c.c. of normal physiological salt solution. The solutions used for administration per os, consist of a solution of radium chloride in two ounces of distilled water, each bottle of the solution containing two micrograms (0.002 mg.) of radium element.

"A study of the effects of radium on the metabolic processes in normal man is being made by one of us and the study of the elimination of intravenously injected radium was made on the subject of this metabolic study. A normal man of about 23 years, who had been on a diet, was given 100 micrograms of radium (element) by injection into the cephalic vein, on December 11, 1914. Table I shows the elimination of radium in the feces and urine."

---

\*Seil, Viol and Gordon—Radium v; 40-41, May, 1915.

# RADIUM

Table I.

Day	Micrograms radium element in Feces	Urine	Combined	Micrograms radium remaining	Per cent. rate of elimination of radium
1	Injection 100 micrograms radium element.				
2	17.9	1.75	19.65	80.35	19.65
3	16.6	0.22	16.82	63.53	20.9
4	7.12	0.065	7.185	56.34	11.3
5	1.6	0.040	1.640	54.70	2.9
6	1.6	....	1.6	53.10	2.9
7	0.98	....	0.98	52.12	1.8
8	0.58	....	0.58	51.54	1.1
9	0.44	....	0.44	51.10	0.85
10	0.42	....	0.42	50.68	0.82

"The radium determination were made by the radium emanation method using aliquot parts of the feces and urine."

"From the data in Table I it is clear that at first there is a rapid elimination of the radium, mainly in the feces. The absolute amounts of radium eliminated from day to day will depend somewhat on the quantities of feces and urine excreted. Since the radium salts are not volatile, the only other manner in which they might be eliminated is in the skin secretions. The radium eliminated in the urine is so much less than that in the feces that it is not unreasonable to expect that the amount eliminated through the skin would be very small. Radium is an element closely related chemically to barium and the other metals of the alkaline earths, strontium and calcium. From chemical considerations it would be expected that the radium held in the body, would be found wherever other alkaline earth elements are found. The bones should therefore contain the largest amount of the radium, and analysis in many cases shows that the bones do have the highest concentration of radium of any of the tissues. Following the bones, in the order of concentration of radium, come the liver, lungs, blood vessels and spleen. The explanation of the rapid fall in the daily rate of excretion of the radium from 20 per cent of the radium present during the first two days to less than one per cent of the radium present at the tenth day (cf. last column in Table I) lies in the gradual absorption of the radium in the various tissues. When injected into the blood stream the quantity of radium (0.1 mgm. radium element equaling 0.13 mgm. of radium chloride or 0.14 mgm. radium sulfate) is so small that it would hardly give a visible precipitate in the form of sulfate. As a result the radium is carried in solution or suspension in the blood until it either becomes absorbed by the various tissues in proportion to their alkaline earth salt content and to the accessibility of the blood to the organ, or is eliminated."

"To check the results in Table I, a similar intravenous injection of 100 micrograms of radium was made in the same man, February 3, 1915. By this date the radium eliminated as a result of the first injection on December 11, 1915, was assumed to be negligible, and the analytical results as given in Table II show this to be the case."

Table II

Day	Micrograms Feces	Micrograms radium element in Urine	in Combined	Micrograms radium remaining	Per cent. rate of elimination of radium
1	100 micrograms radium element injected.				
2	18.4	1.4	19.8	80.2	19.8
3	12.58	0.16	12.74	67.4	15.9
4	3.34	0.065	3.40	64.0	5.0
5	1.68	....	1.68	62.3	2.6
6	0.54	....	0.54	61.8)	
7	1.67	....	1.67	60.1)	Av. 1.8
8	0.45	....	0.45	59.7	0.75
10	0.30	....	0.30	ca. 59.0	ca. 0.5
12	0.30	....	0.20	ca. 58.5	ca. 0.34
21	0.14	....	0.14	ca. 57.0	ca. 0.25

"These results are in good accord with the data in Table I."

"To determine the rate of elimination of radium taken per mouth, one of us (S.) ingested a solution containing 50 micrograms of radium element. Through a blunder on the part of a janitor the feces samples for the first two days were interchanged and the sample for the second day was thrown out before the exact weight was determined. The data in Table III therefore are in part only approximate and are recorded simply for a comparison with the data obtained in a similar experiment, made later, the results of which are given in Table IV."

Table III.

Elimination of Radium. 50 micrograms of radium element taken by mouth. March 2, 1915.

Day	Micrograms Feces	Micrograms radium element in Urine	in Combined	Micrograms radium remaining	Per cent. rate of elimination of radium
1	Radium taken at mid-night.				
2	7.6	0.124	7.72	32.38	15.4
3	ca. 16.0	0.15	ca. 16.0	ca. 16.28	ca. 50.0
4	2.9	....	2.9	ca. 13.38	ca. 18.
5	0.38	....	0.38	ca. 13.0	ca. 3.

Table IV.

Elimination of Radium. 50 micrograms radium element taken by mouth. March 9, 1915.

Day	Micrograms Feces	Micrograms radium element in Urine	in Combined	Micrograms radium remaining	Per cent. rate of elimination of radium
1	Radium taken about mid-night.				
2	17.9	0.102	18.0	32.0	36.0
3	12.2	0.013	12.2	19.8	38.1
4	12.19	....	2.19	17.61	11.0
5 & 6	0.626	....	0.626	16.98	3.5

"Radium taken into the body is continually disintegrating with the formation of the gaseous radioactive substance, radium emanation. This gas is carried by the blood to the lungs, where the emanation passes out of the blood by diffusion, and is lost from the body in breathing. The amount of emanation in the exhaled air was measured after the first



# RADIUM

experiment on radium taken by mouth, the data in Table V being a record of the results."

Table V.

Concentration of radium emanation in the exhaled air, after taking 50 micrograms of radium (element) by mouth. March 2, 1915.

Day	Hour	Radium emanation per liter of air	
		in mache units.	in milli-microcuries.
March 3	10:40 A. M.	0.588	1.59
3	4:50 P. M.	0.551	1.40
4	10:30 A. M.	0.182	0.49
5	2:50 P. M.	0.070	0.19

## CONCLUSIONS

"Taken by mouth a much greater part of a soluble radium salt is eliminated during the first three or four days, but after that, the rate of elimination is sensibly the same as when the radium is introduced by intravenous injection."

"The main part of the radium is eliminated in the feces. When the radium is taken by mouth, a smaller proportion of the excreted radium is found in the urine than when the radium is injected intravenously. From 25 to 35 per cent of the radium taken by mouth remains in the body four or five days after ingestion. From 55 to 65 per cent of the radium injected intravenously remains in the body four or five days after the injection. From this time on the elimination proceeds at about the same rate in each case. By the tenth day after taking the radium the daily rate of excretion is less than one per cent. This results in an exceedingly slow elimination of the last of the radium, the process going on for months. The first rapid elimination takes place before the radium has been "fixed" in the tissues. After that has taken place the excretion is much slower, and even the amount of emanation which is given off, is less. It is a well known fact that a solution of radium salt can be completely de-emanated by passing a current of air through the solution. Even the dry radium chloride and bromide (soluble salts) give up quite large proportions of their included radium emanation. Insoluble radium sulfate, even when finely divided, holds the emanation very strongly, so that less than 5 per cent of the emanation escapes from the salt."

"From the above results, a rational method for maintaining a certain amount of radium in the system can be suggested. If, for example, it is desired that about 50 micrograms of radium be maintained in the body—an intravenous injection of about 100 micrograms is made, and after 10 days, it will suffice to take 2 micrograms of radium by mouth, every few days, in order to make up for the radium being lost. Radium solutions taken by mouth repeatedly will have a cumulative effect. However, the elimination of radium taken by mouth is about twice as rapid as when the radium is injected intravenously. Therefore, there will be required about twice as much radium to produce a given result, when the radium is taken by mouth. This is in accord with the clinical findings of many workers, who have obtained results more rapidly with smaller total qualities of radium injected intravenously than with larger total qualities of radium taken by mouth."

## AN INSTRUMENT FOR THE APPLICATION OF RADIUM TO THE TONSILS

By CLARKE WALLACE STEWART, M.D.  
Olean, N. Y.

Figure 1 represents a new instrument for the application of radium to tonsils in the treatment of both enlarged and diseased tonsils and adenoids. Constructed of very light metal, its total weight amounts to but very little. Its ready adaptability to the patient's tonsil and ease of removal, in case of gagging, or for any other reason requiring its quick removal; its stability of parts and ease of sterilizing are points of advantage.

The instrument consists of a so-called tooth plate and groove with two prongs extending forward on either outer edge of the tooth plate. The central bar is notched in the median line and has at its posterior end a receptacle for holding the radium container. This notched bar allows for the proper adjustment of the distance between the teeth and the tonsil and keeps the radium against the tonsil being treated. A small rubber band is placed over the central bar and over either one of the projections desired at the side of the tooth plate, the elasticity of the rubber band allowing snug contact of the radium container against the tonsil being radiated.

The radium container has a swivel attachment that allows the container to be moved to either the right or left tonsil as desired.

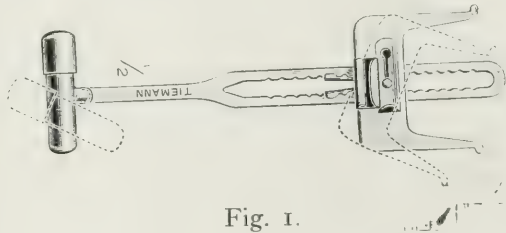


Fig. 1.

Some patients find it difficult to swallow the saliva with the instrument in situ and will drool like a baby. The saliva can be absorbed by either office towels or absorbent pads placed against the chin—a better method would be to use a suction tube such as the dentists use in their work.

I have found this little instrument of very great convenience in my work upon diseased tonsils and adenoids. It is made by the George Tiemann Company at 107 East Twenty-eighth street, New York. I have no patent upon it and gladly dedicate it to the use of other radium workers.

In the treatment of tonsils, in old or young, I use a thirty milligram tube of radium generally for one hour each treatment, giving the treatments every other day, treating each tonsil alternately until each has been given six treatments. At the end of this time I put my patients off for about eight weeks when they return for inspection.

If the reduction of the tonsils is not complete I then give another series of treatments. As a rule the first series of treatments is sufficient for a complete cure. The follicles seem to turn inside out as the tonsil

## **RADIUM**

tissue shrinks and all that is left of the tonsillar tissue, as a rule, is a little shrunken nodule about the size of two peas and this result is permanent.

Occasionally I find a patient in whom an hour's treatment creates too great a reaction and upon these patients, for the first two or three treatments, I use the radium for a shorter length of time.

I have never had a reaction that caused any particular inconvenience, and, as a method for the cure of enlarged and diseased tonsils and adenoids, I am convinced, after having observed a large number of cases over a period of about two years, that it is far superior in its results to that of surgery and is absolutely free from all the dangers that accompany surgical measures.

The radium seems to have a special predilection for the tissues forming the tonsils and adenoids and causes them to shrink, but this action has not been observed in the other tissues of the throat.

The treatment is painless and safe. I anaesthetize the throat by simply spraying with an ordinary solution of novocaine, which acts quickly, and then I immediately apply the radium.

An elongated uvula can be caused to shrink in the same way, but it does not respond as readily as the tonsils and adenoids.

In children the respiratory relief and freedom from mouth breathing is quickly apparent. The little, weazened pinched face soon fills out, and the general health greatly improved. In all patients, old or young, there is prompt relief from throat infections and which seem to be more difficult to acquire. The disappearance of the follicles and crypts of the tonsils give relief from follicular tonsilitis and quinsy. The lymphatic channels are closed and do not afford transmission of bacteria and their products to the other tissues of the throat and lymphatics of the neck.

The well being of each patient has been marked and there is a very noticeable freedom from the usual throat troubles even before the series of treatments are completed.

I cannot recommend too highly the use of radium in the treatment of enlarged and diseased tonsils and adenoids.

I feel certain that this instrument will be welcomed by the radium workers in their treatment of tonsil cases.

---

## **RADIUM AND THE INCOME TAX**

GEORGE E. PFAHLER, M.D.,

Past President, American Radium Society.

At the St. Louis meeting of the American Radium Society, the late Dr. Russell H. Boggs and I made a real effort to get recognition of radium as an office expense, or to obtain some depreciation value. We foresaw the possibility of our radium decreasing tremendously in value. As a matter of fact, it has decreased in value fifty dollars a milligram, which receives no recognition from the government unless the loss is established by sale. We employed Mr. Charles M. Johnston to present this matter at Washington, together with a petition signed by the radium owners; and I give herewith his final report.



Dear Dr. Pfahler:

Pursuant to the instructions of yourself and Dr. Russell H. Boggs, of this city, I at once began the preparation of a petition to be filed with the Internal Revenue Office at Washington, requesting a modification of the present ruling on radium.

The untimely death of Dr. Boggs was a real misfortune in this matter, as he was very familiar with many facts that would certainly have had weight with the Department at Washington. However, after considerable labor and investigation, I prepared a petition asking that the present ruling be modified either by permitting the cost of radium to be charged as a current expense, with a provision to the effect that in the event of the subsequent sale of the radium the selling price would be charged as income, or that a depreciation allowance be allowed each year on all radium held by physicians and used for therapeutic purposes.

The petition was very lengthy, covering about ten typewritten pages, and later, a five-page supplement, amplifying some of the arguments in the original petition, was added. Both the original and the supplement were presented by me to Commissioner Blair, of the Internal Revenue Department, and one of his assistants, Mr. Mattox, at Washington, at a conference on this matter that lasted upwards of two hours. I had attached to the petition the copy of the resolution passed at the meeting of the society in St. Louis, and also the original petition signed by the physicians individually at the same meeting. I went carefully over all the matters set forth in our petition, resolution and the physicians' petition, with the above-named gentlemen, and was shown every consideration and courtesy by them. Unfortunately, however, they were unable to grant us relief.

The decision, a copy of which is hereto attached, explains the position of the Commissioner in detail.

For your information and for the information of any physicians not familiar with the present ruling, I am also attaching hereto a copy of the present ruling, O. D. 837, cited in the Commissioner's decision.

Yours very truly,

CHARLES M. JOHNSTON.

DECISION OF INTERNAL REVENUE COMMISSION ON APPLICATION  
FOR CHANGE IN RULING ON RADIUM

Reference is made to your recent request on behalf of the American Radium Society and of other owners of radium in the United States for a reconsideration of O. D. 837 in which it was held that the cost of radium used as a therapeutic must be treated as a capital expenditure and that radium is not subject to depreciation.

You state that owing to the great cost of radium, the experimental character of its use, and difficulty in selling it and the possibility of the discovery of some method of treating cancer which will decrease the market value of radium you consider that a depreciation allowance of fifteen per cent should be granted or that physicians using it should be permitted to treat the cost as a business expense in the same manner as the cost of drugs.

The motives of policy which you have suggested such as the desirability of encouraging the use of radium and preventing the commercialization of its use may not be taken into consideration by this Bureau in administering the Federal Income Tax laws, however excellent these motives may be. The test of the allowance of this deduction is the same as the test of the allowance of every other deduction and depends

## RADIUM

upon whether it meets the requirement of the statute. The Bureau is without authority to set aside the express provisions of the Revenue Act of 1921 or any other revenue act even if the administration of these provisions imposes a hardship upon the taxpayer or group of taxpayers.

The provisions of the Revenue Act of 1921 relating to depreciation are set forth in Section 214(a) (8) which provides for the allowance of:

"A reasonable allowance for the exhaustion, wear and tear of property used in the trade or business, including a reasonable allowance for obsolescence. In the case of such property acquired before March 1, 1913, this deduction shall be computed upon the basis of its fair market price or value as of March 1, 1913."

Under this section the allowance of depreciation is limited to such property as is subject to "exhaustion, wear and tear," that is, to property that has a life extending beyond a year but is not of such indefinite life that the depreciation which it sustains is negligible. The measure of depreciation is based on the probable life of the property as determined from its character and use.

An arbitrary deduction of fifteen per cent for depreciation, therefore, is not allowable as the depreciation of radium cannot possibly be based on a probable life of six and two-thirds years. On the contrary, as it was set forth in O. D. 837, the life of radium is so indefinite that depreciation is negligible.

It is also not possible to allow the deduction of the cost as an item of expense. Inasmuch as radium is not a material consumed or worn out through use during the taxable year, it represents a capital expenditure which under Section 215(a) of the Act is not deductible.

With reference to your statement that the discovery of a new method of treating cancer may result in rendering the use of radium obsolete, you are advised that in the event of its becoming obsolete a deduction for the loss of useful value may be claimed in the return for the year in which its use is abandoned. If the radium is sold at a loss either by a taxpayer or his estate, the loss may be claimed as a deduction from any income received whether from professional services or other sources. For this reason it is not believed that any undue hardship is imposed upon physicians using radium for treatment by the application of these principles.

In view of the express provisions of the statute it is not considered that O. D. 837 should be modified or reversed.

Respectfully,

C. P. SMITH,  
Acting Commissioner.

### PRESENT RULING

Since the full life of radium has been scientifically estimated at such an extended period and since no appreciable depreciation results from its continued use as a therapeutic agent, the depreciation occurring during the lifetime of any individual owner is practically negligible. It is held, therefore, that radium which is used as a therapeutic is not subject to depreciation for income tax purposes and its cost must be treated as capital expenditure. The return of capital will be realized upon its sale or other disposition.

Cum. Bul. No. 4, June, 1921.

Treasury Dept. Page 178.

Office Dec. 837.

Ruling 10-21-1496.

## REVIEWS AND ABSTRACTS

William S. Stone, M.D., (New York City). The Present Field for the Use of the X-Rays and Radium in the Treatment of Malignant Neoplasms. Amer. Jour. Roentg. ix, 502-507, August, 1922.

"Roentgen rays and radium in the treatment of malignant neoplasms are still accepted reluctantly by the surgeon, except as palliative agents in the advanced stages of the disease. Their application before the patient is in an incurable stage appears to be an insufficiently tested method. In the case of x-rays, it is particularly so, for, before the recent advent of the high voltage machine, x-ray therapy had become so overshadowed by the results of radium that it had lost somewhat of its early reputation."

"It seems, therefore, to be an opportune time to review this work, as it has been presented to the writer during a service of seven years at the Memorial Hospital. During this period more than 10,000 cases of neoplastic disease have been under his observation, to the majority of which x-rays or radium has been applied. We feel that we have now arrived at a position in this work from which we may discuss *the surviving old, the established new, and the still experimental.*"

"As to the *surviving old*, the operation no longer maintains its former position of being the only method of treating cancer in the curable stage. It is no longer in many fields the method of choice. There still remain, however, numerous fields in which our enthusiasm for the physical agents must not allow the postponement of the operation to lessen or take away its chances of success. In all the well-advanced cases, and in those designated as being in the borderland of operability, in which formerly a radical operation was attended by a high primary mortality and a low percentage of cures, the surgeon's responsibility is not fulfilled until all the aid has been enlisted which x-rays and radium can supply. In fact, there are few, if any, early cases of malignant neoplasm, in which these agents do not merit consideration, if only as an adjunct to the operation. In other words, the surgeon's position as a technician has been made easier, but from the viewpoint of diagnosis and proper selection of cases, his responsibility has become greater. Even in diagnosis, the therapeutic test of irradiation will often render an exploratory operation unnecessary. Instead, therefore, of being supplanted by these agents, the field of applicability of the operation has been limited strictly to the earliest stages, by which, also, we may hope to define more accurately its curative value."

"Of the *established new*, we now have numerous facts relating to the conditions upon which the effects of irradiation depend. While the early observations have been confirmed, that tumor cells, in general, respond more promptly to the action of the x-ray and radium than the normal tissues, such wide variations are shown among the different types of tumors, even between tumors of the same type in different parts of the body, that we can hardly appreciate the basis for speaking of a carcinoma or a sarcoma dose. Just as wide variations also occur among the sarcomas as among the carcinomas."

"The effects of irradiation depend upon the size, extent and condition of the tumor. The size, however, is of less importance than with the operation, some of the bulkiest of abdominal tumors, for example, disappear within a few weeks. The extent of the tumor is also of less importance but an extension to a neighboring bone, unless the tumor



## RADIUM

is of the most responsive type, will seriously interfere with the result."

"The condition of the tumor and its neighboring tissues, next to its type, determines the success or failure of irradiation more than any other factor. Infected tumors respond unfavorably, and a syphilitic base, in a lesion of the tongue, for example, invariably hinders the progress of the regression. A tumor also with altered nutrition, in which the general condition of the patient may still be apparently good, may soon become so necrotic from the irradiation that the terminal period of the disease is prematurely initiated. The fear of toxicity, however, from the absorption after irradiation of the products of disintegration in a normally nourished tumor has been, I believe, somewhat exaggerated in the literature. Fibrosis resulting from an operation or a previous irradiation makes a tumor less responsive. The greater effects of these agents upon tumors and normal tissues which have not been previously irradiated is universally accepted by all observers. The existence of normal neighboring tissues and their preservation by the avoidance of overdosage constitute an important factor in the process of cure. The killing of the cancer cell is only one of the essentials, to which must be added a proper amount of inflammatory reaction on the part of the stroma of the tumor and normal tissues. For this reason, also, a poor condition of the general health, altering the nutrition of the tissues about the tumor, makes conditions which are unfavorable for regression of the tumor."

"The general health of the patient must be considered, also, because of the toxemia which necessarily results from the application of these agents—a subject which deserves more consideration, especially in the case of elderly people, than it has hitherto received. The effect of these agents upon the blood must also demand our attention. It is not improbable that the cell count may become an aid in determining the intervals between treatments. In observing the general condition of the health, it is necessary to distinguish between a condition resulting from hemorrhage or toxicity from a necrotic tumor, and the cachexia from the generalization of the growth. In the latter condition, any treatment is contraindicated, but in the other conditions a stoppage of the hemorrhage or the removal of a necrotic focus may enable irradiation subsequently to produce satisfactory results."

"Much confusion exists regarding the relative merits of x-rays and radium, but so far as we are able to judge clinically, the effects of x-rays and the gamma rays of radium are the same. With a supply of 4 gm. of radium, however, we have been able to obtain more marked effects upon deeply situated tumors than we have from the use of the x-ray machines delivering not over 100,000 volts. The effects of each depend upon the power of absorption the tissues possess for rays of certain wave-length. Some of the gamma rays, we know, are of such short wave-length that they penetrate the tissues without being absorbed, and without, therefore, producing therapeutic effects. We hope, then, to obtain from the transformer producing a higher voltage a quantity of x-rays of sufficiently short wave-length to make this agent an efficient substitute for radium in cases in which deep effects are required. It will be an error however, to undervalue the therapeutic effects that have already been obtained by the use of the lower voltage machines. Numerous cases do not require rays of shorter wave-length than these can produce, and with a technique in which distance, filtration and time are increased materially, we await improved results with the old machines."

"A review of the material from which these general facts were obtained enables us to present numerous clinical fields in which, although the response to irradiation varies widely, the results indicate that x-rays and radium have a specific field of applicability."

"Lymphosarcoma, metastatic teratoid tumors of the testicle, certain embryonal tumors of the kidney in children and a type of bone sarcoma recently described by Ewing as endothelial myeloma, represent types of neoplasm which promptly respond either to the gamma rays of radium or x-rays after a single application. The unfortunate results of biopsy or operation in lymphosarcoma may be avoided by the therapeutic test in cases of a doubtful nature. The metastatic teratoid tumors of the testicle are even more responsive than lymphosarcoma, but we are not yet prepared to offer definite conclusions regarding the treatment of the primary tumor. For the present, we think it should be excised after a preliminary irradiation. We have observed only a few embryonal kidney tumors in children, but in each case the regression has been favorable. The endothelial myeloma may be best discussed with the other bone tumors, but the response to irradiation is so similar to lymphosarcoma that they are included in this group."

"There are other tumors in which the response to these agents is often prompt, but the results vary. *Mixed tumors of the parotid*, depending upon their individual structure, vary widely, but on account of the nerve palsy and deformity that so often follow the operation, a preliminary trial of irradiation should always be made."

"The results in basal cell epithelioma, or rodent ulcer, discovered by the pioneers in x-rays to be susceptible to that agent, have been so greatly improved by radium that operation is rarely indicated. Errors in diagnosis, however, are easily made, and the condition of the growth has been so often altered by unsuitable previous treatment that it may be wise to give a guarded prognosis. In lesions near the eye, in which ectropion so invariably follows the operation, the superiority of radium is well known."

"There is a large field of ulcerating growths of the skin and mucous membranes, in which, by the additional use of the beta rays and by implantation of radium into the tumor tissues, results have been achieved in many instances beyond those that have hitherto been accomplished by the knife or cautery. In this way, during the past three years, lesions of the lip, tongue, mouth, tonsil, larynx, etc., have been brought into a group in which the operation has been supplanted, practically, by the use of radium. This use of radium, however, is taking advantage to some extent of its caustic qualities, concerning the action of which there remains much to be investigated. In all these lesions, especially of the lip and tongue, the regional invasion of the lymph-nodes presents the most difficult part of the problem, for the solution of which a judicious combination of surgery and these agents is required. For the performance of this work considerable experience in their use, and radium in a suitable form, are necessary, so that the choice of procedure may depend upon the amount of experience in the use of these agents that the patient is able to command."

"In uterine cancer, radium has achieved its most brilliant success as a curative agent, especially in lesions of the cervix, in which surgery has now a very limited field, if any, of applicability. The results of surgery, however, in early lesions of the uterine body are so good that, for the present, at least, operation after a preliminary use of radium appears to be the method of choice. A most conservative statement

## RADIUM

would be that any uterine lesion requiring more than a simple hysterectomy for its cure should be treated by radium. Our experience with the x-ray does not justify our reliance upon this agent alone in the treatment of uterine cancer. Even in Germany, there have been only a few cases, I believe, in which radium has not been used in connection with x-rays."

"The results in all the other growths of the mucous membranes fall short of those we have just discussed. There is little evidence of practical accomplishment in cancer of the esophagus and stomach. Our primary results in tumors of the bladder, because of the frequency of their papillary and non-infiltrating character, justify the expectation that these agents will have definite curative value. There is already no doubt of the palliative value of radium. There is also much evidence of its palliative value in cancer of the prostate, but special care is needed in the selection of cases, because the treatment temporarily adds to the patient's discomfort, and the prolongation of life must, therefore, be sufficient to justify the attempt."

"Cancer of the rectum has proved a more difficult problem than our first results led us to expect. The extreme sensitiveness of the normal mucosa makes it difficult to give a sufficient dosage, and in an annular growth a permanent stricture is practically impossible to prevent. Life in such instances may be prolonged, but it is usually at the expense of suffering. In any serious effort to cure this lesion by irradiation a preliminary colostomy is necessary. Annular lesions, to be suitable for radium treatment, must be practically of the same early type in which the operation is indicated. In lesions limited to part of the circumference of the rectal wall, surface irradiation combined with the implantation of radium in the growth, and followed subsequently by excision, has produced better results than could be obtained by the operation alone. Cessation of bleeding and pain in a few advanced lesions have been accomplished by the use of the gamma rays. It may be that x-rays will accomplish much better results."

"There is little need of discussing the applicability of these agents to inoperable and recurrent lesions, except to direct attention to the abuses, which the circumstances surrounding the patients in these stages of the disease so often lead us to practice. It is surprising how long an interval will elapse before a patient with a recurrence is referred to a radiologist, whereas there is the same necessity of treatment in the early stage as there is in the case of the primary growth. Neither agent is applicable for the terminal period of the disease. It too often happens that, instead of receiving morphine and good nursing care, the patient is dragged about in the forlorn hope of being helped by x-rays or radium. Both the surgeon and radiologist are responsible for these abuses. The surgeon, whose enthusiasm for the use of irradiation may only begin when he sees the opportunity of avoiding a disagreeable situation, too often emphasizes its value then, and the radiologist is able only to carry out what he knows to be a hopeless undertaking. The performance of an incomplete operation before the case is referred to a radiologist is fortunately becoming less frequent. In New York, we have seen this most frequently in the case of uterine cancer, in which the removal of the uterus materially lessens the value of irradiation. However, in the proper selection of cases, some of the most advanced growths have yielded to irradiation in a remarkable way. As with the primary tumor, success depends upon the type, size, extent and condition of the growth. Regarding metastases, the writer has been fortunate in observ-



ing favorable results following the application of the gamma rays of radium to bone metastases from mammary cancer. There appears to be more than an even chance of relieving pain, and in a few instances, the repair of the lesion, as shown in the roentgenograms, and a temporary restoration of the general health have justified our efforts."

"Of the *still experimental*, it may fairly be said that all this work is experimental, because, even in the fields where much has been established there is much more awaiting both laboratory and clinical research. There are a few clinical problems, however, in which we are now especially interested."

"The prophylactic use of irradiation before and after operation is, perhaps, one of the most important, and cancer of the breast, although much has already been established regarding the irradiation of this tumor in its advanced stage, presents a profitable field for the discussion of this subject. Growths of these organs vary widely in their nature and in their response to irradiation. We have observed that a few primary tumors apparently disappear after the application of x-rays and radium. A partial regression has been observed in a large number, and after repeated applications they have shrunk to an inactive lump. We have also seen tumors inoperable because of their extent and fixation become transformed into tumors that were apparently operable. As our technique has improved, and radium has been implanted in the tumor tissues, much better results have been observed, so that a few cases, in which for special reasons the operation was contraindicated, we have trusted to irradiation alone. From such observations we must conclude to make use of these agents in conjunction with the operation during the early stages of the growth."

"The postoperative application is becoming a routine procedure, and it is reasonable to believe that an increased number of permanent cures will result. We do not yet know, however, how soon after the operation to begin treatment, how often to apply it, how long it should be continued, or what dosage to apply. We have assumed that it will do no harm. Recurrences take place in spite of this treatment, and, according to the writer's experience with irradiation of Hodgkin's disease, nodes, which appear in areas that have been prophylactically irradiated do not respond as promptly as those occurring in areas that have not been previously treated. In Hodgkin's disease, also, after irradiation over long periods, injurious effects have been demonstrated at the autopsy table, on normal structures. In a case of mammary cancer, one year after operation, in which a few supraclavicular nodes had been the only evidence of the disease for several months, one application of x-rays to the chest wall and neck was followed in ten days by a rapidly fatal recurrence in the chest wall and pleura. While such observations do not condemn the procedure, the necessity is suggested for closer study of the effects of these agents upon normal tissues."

"The pre-operative treatment of mammary cancer is much less popular, but it appears to the writer to rest upon a more scientific basis than the postoperative application. From our own observations we must believe that the injurious effects of the operation are thereby minimized. Numerous objections, however, to this procedure are offered by the surgeon, a few of which deserve our discussion. The objection that the healing of the wound is delayed, is based apparently upon a few scattered observations. On the contrary, a prominent surgeon recently stated that after irradiation he observed that wounds healed better and left a better scar. A greater liability to wound infection appears to

have some basis of fact. The writer has made several observations of a peculiar erysipeloid skin infection, occurring several weeks after treatment in the presence of an open wound, which suggests a relationship to the previous irradiation. The objection that the operation is made more difficult is the one most frequently offered, but, in the case of the breast, except for a slightly increased tendency to hemorrhage, if performed too soon, it is difficult to conceive that such an objection is valid. It is most often observed in connection with the performance of a hysterectomy for uterine cancer. It is usually based in this field upon an erroneous conception of the extent of the lesion before treatment. If there has been little or no extra-uterine tumor tissue, there will be no hard tissue to cut through. If, however, as a result of the irradiation, a considerable amount of extra-uterine tumor tissue has been converted into a fibrotic scar, the operation will naturally be difficult. A correct conception, however, of the original lesion would have shown that the operation was contraindicated. The general adoption of pre-operative treatment in mammary cancer will soon show, I believe, that the field of applicability of the radical operation should be much restricted. It already seems to the writer that the presence of hard, fixed nodes in the apex of the axilla makes the cases as unsuitable for a radical operation as does the presence of supraclavicular nodes. It is a question how long it will be before the *radical* operation in mammary cancer will be entirely discarded."

"The use of the x-ray and radium in the treatment of primary bone sarcoma is in the experimental stage, but a few facts have been definitely established, and our results suggest that, with greater accuracy of diagnosis, with an improved technique, and with more frequent resort to the use of these agents prior to operative procedures, more substantial progress will be made. First, our work has confirmed the experimental results of the physical laboratory which show that the bone structures offer but little more resistance to the penetration of the rays of these agents than the soft tissues. The most substantial evidence of this is seen, in addition to the clinical improvement, in new bone production as demonstrated in the roentgenograms. As in the soft tissues, we have found that the effects depend upon the nature, size, extent and condition of the tumor. Infection and necrosis from overdosage are greater obstacles to success in bone tumors than in tumors of the soft parts. Bone tumors that responded well at first did badly after they had become infected. The type of the tumor is the most important factor."

"In the malignant osteogenic tumors, which were most often of the periosteal type, our clinical results were practically negligible, except in one or two instances. In numerous cases, however, the evidence of new bone production, although often slight and temporary, in the roentgenograms showed that effects had been produced; and it leads us to hope that, by irradiating such tumors prior to amputation, the final results will prove to be better than they were when the operation was the only resource."

"In the giant-cell tumors, or relatively benign giant-cell sarcoma, varying in type from those which closely resemble the osteitis fibrosa or bone cyst, to those in which their local extension and recurrence show considerably malignant qualities, our progress has been both encouraging and disappointing. Radium has been applied to the wound after curettage to prevent recurrence, and in numerous instances, the local recurrences after the operation, either by surface irradiation or by implantation into the tumor, have completely disappeared. Necrosis and

infection, however, have often made the progress of repair slow, and, in a few cases failure of the wound to heal, although the growth had been stopped made amputation finally necessary. The results of the use of x-rays or the gamma rays of radium in tumors of this type, which were inoperable on account of their location, lead us to think that, with their earlier recognition by means of the clinical history and x-rays, this form of therapy may ultimately prove to be an efficient substitute for incision and curettage."

"In the progress of this work a tumor presenting many of the features clinically of a malignant periosteal sarcoma responded primarily to irradiation by the gamma rays of radium as promptly as lymphosarcoma. A similar response occurred in several other cases of bone tumor, all of which showed the same histological features, and which Ewing has described as endothelial myeloma. Although they differ from the characteristic features of each of these tumors, histologically and clinically they resemble both. From the x-ray standpoint they resemble giant-cell sarcoma and myeloma, but differ from each. In the long bones they begin in the shaft. Clinically, they occur in youth, are often multiple when first observed, and in general, present the picture of a malignant tumor. They are usually described as round cell sarcoma of the bone. If, like myeloma, they have a multiple focus of origin, we may expect nothing more than a palliative result, which we obtain by the use of irradiation in that disease."

"In conclusion, in addition to supplanting the operation as the method of choice in a number of fields of malignant neoplasm, the use of irradiation has so limited the field of applicability of the *radical* operation in numerous others that it is becoming a questionable procedure. In uterine cancer, it is entirely eliminated, and, in mammary cancer, it is a question of accurate diagnosis."

"The use of irradiation, therefore, has made greater refinement in diagnosis necessary."

"To this end, the patient's interests are best conserved by obtaining the conjoined knowledge of the surgeon and radiologist. In fact, cancer therapy has become an institutional problem requiring more clinical experience and knowledge of surgical pathology to use physical agents than does the operation."

\* \* \* \* \*

George E. Pfahler, M.D., (Philadelphia, Pa.), The Effects of the X-Rays and Radium on the Blood and General Health of Radiologists. American Journal Roentg. ix, 647-656, Oct., 1922.

"The report of five deaths\* from aplastic anemia, due directly or indirectly to the radiations of radium or x-rays, is of deep personal interest to every radiologist. Even though these deaths are not fully accepted as being due directly to the radiations, still it has seemed to me advisable that we, as American radiologists, should take account of our present status. If we are in such danger, it is clearly evident that we must take sufficient additional precautions to avoid such accidents. Even if, as a whole, we are sufficiently protected and sufficiently cautious, there may be individual workers who are taking unnecessary risks."

"If we are not running any such grave risks, we must not add further to the unjust prejudice against us on the part of life insurance companies, which is apt to form as a result of such reports. Some companies actually refuse to issue insurance to those engaged in radiological practice, because of the accidental deaths which have occurred in those who were exposed excessively in the early days of roentgenology,



## **RADIUM**

when the dangers were unknown, and the means of protection undeveloped."

"The insurance companies should realize that they have not actually lost money because of these deaths. The development of every powerful agent for good leads to the sacrifice of some lives, but the saving and prolongation of other lives compensate a hundred-fold for these losses. These pioneers in radiology sacrificed their lives in the development of this branch of medical science, but I am sure I can say truthfully that for every death more than a thousand lives have been saved, and many thousand prolonged, because of the benefits which have come from the aid given in diagnosis and treatment. I believe no one will dispute this. Then the insurance companies have gained in actual cash, because of the prolongation of premium paying, and the prolonged use of the money invested. Therefore, instead of their prejudice, there should be an everlasting debt of gratitude."

"Preceding these five cases referred to above, the deaths of radiologists from excessive radiation have been due to the development of malignant disease secondary to the chronic irritation of the skin. This skin irritation has been practically eliminated, or at least the means and knowledge are at hand to give protection against such effects. Those entering the field of roentgenology or radiation therapy during recent years should be free from all such effects. For this second reason, present-day prejudice of insurance companies against radiologists is unjustified."

"As the amount of radium used in medical practice increases, and as the x-rays are being made more powerful, we may be facing new dangers. It is better that we investigate now."

"The deaths of three workers at the Radium Institute of London have been attributed to their occupation. The first death occurred in December, 1916, in a worker who was seen by several eminent specialists, and whose death was ascribed by them to pernicious anemia. The second death occurred in January, 1920, in a nurse, and was due to infective endocarditis, but it is admitted that the radium had unquestionably affected her, though it was not from this alone that she died. The third death occurred in February, 1921, in a man, aged forty-seven, and was due to acute pneumonia. Each case is claimed to have been due to a definite disease apart from the effects of radium, but the Institute Committee consider it highly probable that the work of these persons weakened the power of resistance to the diseases from which they suffered."

"Larkin reports a fourth case in which the disease was ascribed to the effects of the x-rays. A male, aged forty-three, had been working at radiography for fifteen to eighteen years. He was of excellent physique, and for eighteen months had been putting on weight; his general health had never been better. His complexion had always been sallow, a fact which unfortunately masked the onset of the fatal anemia. In October, 1920, a blood examination casually made showed Reds, 4,200,000; Whites, 7,200; Hb., 85 per cent; Diff. L., 38 per cent; P., 60; E., 1.7 per cent. This was three months before he complained of symptoms, and five months before death. In January the patient's color changed to a lemon yellowish tinge, and he complained of dyspnea and loss of appetite. He still kept on working at high pressure, and refused to consult any one. On February 4, 1921, however, he gave in. His temperature at this time was 100.6 F. at night, pulse 90. He had backache. Blood pressure was 110. Blood count now was Reds, 2,700,000;

Whites, 1,600; Hb. 54 per cent, L., 76 per cent; P., 20 per cent; E., 3 per cent. This showed a serious drop in both red and white corpuscles and a complete inversion of the ordinary percentage relation of lymphocytes to polymorphonuclears. No poikilocytosis, no nucleated reds, and no variation in the size of the red cells were to be seen. Urine showed nothing. He had a hemic murmur, but no evidence of endocarditis. Bacteriological examination of the blood on two separate occasions gave negative results. He grew progressively worse and died March 21, 1921."

"I am referring to this case in a little more detail because the radium cases have received a little more publicity, and some roentgenologists assume that only radium workers need be concerned. In this case there seems to have been no other associated disease. Dr. Larkin remarks that this radiographer had recently changed over from soft to hard tubes for the greater part of the work, and he warns us that the protection that we used for soft tubes is insufficient for hard tubes."

"Foveau de Courmelles refers to a fifth case, Dr. Emilio Tiraboschi, radiologist for fourteen years at the large hospital in Bergamo, making use of hard tubes without precautions, who died in January, 1914, 'in a state of profound anemia. At autopsy upon his body considerable changes were found in the blood, advanced glandular atrophy, and the well-known lesions of extreme exhaustion.'"

"Reviewing the three London Radium Institute cases, and taking into account the great rarity of aplastic pernicious anemia, it might reasonably be concluded that exposure to radium was the important etiological factor. When, however, the blood examinations of other workers is also taken into account, the above conclusion becomes hardly open to doubt. The anemia found was of exactly the same type, only less profound. Add to these facts the constant occurrence of a marked leukopenia, and a complete absence of signs of regeneration, and it is clear that the hematopoietic system of these workers is seriously damaged. The aplastic pernicious anemia found differs from the rare disease of young women in being accompanied by a leukopenia instead of a leucocytosis. In this respect it is similar to certain anemias produced by poisons, as for instance, trinitrotolnol."

"A definite improvement in the blood picture was noted after the workers had been away from radium exposure for several months. Yet, it will be noted in the history of two of the fatal cases, that their symptoms developed after vacations of several months."

"Regaud says operators and attendants can protect themselves by forming the habit of: (1) Taking judicious advantage of the law of distance (especially through the use of special tongs in performing manipulations) and (2) interposing between the operator's body and any source of radiation leaden screens several cm. thick and impervious to penetrating rays. The few accidents that have occurred up to the present time have been the results of ignorance of the danger and lack of precautions."

"Tuffier collected information from various sources and found some complaints of cutaneous lesions, rarely menstrual disorders, azoospermia, and a reduction of polymorphonuclear elements and an increase of lymphocytes in the blood."

Fortunately, the further investigations by Mottram upon the effect of increased protection give us much encouragement. He says: 'Increased protection has now been in operation for six months. As will be seen, this has resulted, with few exceptions, in a return of the blood

RADIUM

conditions to normal." He gives a description of the methods of protection: "It is, however, not enough to provide protections; the workers must know how to take advantage of them. One has heard of a case of a nurse who was accustomed to carry radium each morning from one room to another. She suddenly developed a bad radium burn of the hand, which was accounted for by discovering that some days previously she had had a long conversation with a friend in the passage between the two rooms."

"More recently Mottram has collected 40 blood counts from healthy adults, 20 in radium workers and 18 in roentgen-ray workers, showing the lymphocytes and polynuclear distribution to be abnormally low, particularly in the radium workers. Observations should be made on workers before they are subjected to exposure and then periodic blood examinations should be made. Under these conditions a fall, followed by a sustained low level, would indicate that insufficient protection was being provided. The red cells are not as sensitive to radiation as are the leukocytes, so they make a less delicate indicator. For this reason an anemia must be looked upon as a grave departure from the normal and will indicate a serious overexposure. Red cells are diminished in numbers in radium workers although the color index is high, probably indicative of interference with the production of red cells and polynuclears in the bone-marrow; and observations on the bone-marrow of rats exposed to gamma rays are confirmatory. The penetrating gamma rays of radium react and injure the bone-marrow, whereas the less penetrating roentgen rays exhibit their effects chiefly upon lymphocytes and lymphoid tissues which are not protected by a covering of bone."

"Blood Studies of American Radiologists. In November, 1921, at one of the regular meetings of the Philadelphia Roentgen Society, I proposed that we make a study of our blood. I was then appointed to make these investigations. I decided later to enlarge this plan and solicit the co-operation, if possible, of all radiological workers in America. A blank was prepared, with the co-operation of Dr. John Kolmer, Professor of Pathology, making the following queries:

CLINICAL RECORD FOR BLOOD STUDIES OF RADIOLOGISTS

Name.	Age	{ Physician, Nurse, Technician		
Address.		{ Stenographer, General Assistant		
Name of laboratory.				
Began work.				
	Hours Each Day	Days per Week	Years	
Amount of work.....				
Roentgentherapy.....				
Roentgenography.....				
Roentgenoscopy.....				
Amount of radium handled.				
Do you prepare the specimens?		How?		
Do you apply the radium?		How?		
Describe your protection against the roentgen rays.				
Describe your protection against radium.				
What was your occupation previously,				



Describe your general health before any exposure to rays.  
 Describe your general health or any present symptoms.  
 Mention any causes of present symptoms that occur to you.  
 Record blood pressure.                      S.                      D.                      PP.  
 Record any previous blood pressure tests.  
 Carry a dental film in your pocket for two weeks, marked with a lead number, and mail to me promptly in a tin box, without developing.  
 Record here the results of any blood examinations previously made.  
 Please have a blood examination made as follows at least two hours after previous meal.

	Date	Date	Date	Date
Total erythrocytes.....				
Total leucocytes .....				
Hemoglobin.....				
Differential leucocyte count.....				
Small lymphocytes .....				
Large lymphocytes .....				
Transitionals.....				
Polymorphonuclear.....				
Eosinophiles.....				
Basophiles.....				
Abnormal erythrocytes.....				
Abnormal leucocytes.....				
Blood clotting time .....				

Examined by  
 Remarks.

"One thousand of these blanks were distributed in December, and by request several hundred more were sent out later. Yet only 338 were returned. Probably the most valuable contribution is that made by the medical director of one of our leading radium producing companies. While he requests that his name be withheld, I take the liberty of quoting his 'General Summary of Health Conditions in Radium Workers':"

"Since the establishment of the laboratories that have produced 85 gm. of radium (estimated to be upwards of 60 per cent of all the radium ever refined) there have been no deaths among the laboratory workers. One of the workers, with a continuous service of ten years, had lobar pneumonia in 1919 with a rapid and complete recovery. Another, also with ten years' continuous service, had a general infection (never positively diagnosed) with complete recovery. Five members of the staff who have had constantly to handle radium tubes and needles, are suffering from radium effects on the thumb, index and middle fingers of both hands, produced in the very early history of the laboratory. Since the establishment of regulations that radium must be handled with instruments, this local condition has not progressed in any one of the cases."

"The general health of the laboratory workers is, I believe, above the average. Absence from duty on account of illness is very infrequent. During the 1918 epidemic of influenza, the entire staff escaped almost entirely, there being only one case."

"The general exposure at any one time has amounted to from 200 to 1,000 mgm. of radium in process of crystallization (emanation ex-

## RADIUM

posure), and from 100 to 2,000 mgm. of the finished product (gamma ray exposure). Members of the staff, represented in charts numbered 1, 2, 3, 4 and 5 have received the greatest amount of gamma radiation."

"The average blood count for members of the staff having had the greatest amount of exposure for a longer period than five years, is as

R.B.C.		W.B.C.	Poly.
5,027,500		5,296	63.6 per cent
S. L.	L. L.	Trans.	Hemo.
12.6	22.3	2.5	94 per cent.

Since this tabulation has been recorded, an additional count has been made which in no way differs from the individual counts recorded and tabulated."

"In addition to the above, one of the officers, not directly exposed to radium in the laboratories, has received during the past eight years, 90,450 mgm. hours of gamma ray exposure to a pathological lesion. Treatment consists in the use of from 50 to 200 mgm. of radium used either directly on or buried in the growth. This officer is at the present time in good health, and presents the following blood count:

R.B.C.	W.B.C.	Hemo.
4,250,000	6,200	90 per cent.

The case is quoted as being, perhaps, the largest radium dose on record."

"This report was based upon repeated blood studies which had been made independently during a year, and the study of the individual charts is most interesting. No. 1 and No. 2 had been exposed for ten years, had damaged fingers, and had been exposed to about 85 gm. of radium, yet the blood studies made four times during 1921 showed a normal condition. The lymphocytes were at the low normal level. No. 3, which had nearly the same amount of exposure, showed a variable condition, but in March, July and September there was a moderate leukopenia, and a distinct relative lymphocytosis."

*Male*—Age 35 years—Married—No children.

*Continuous Service*—10 years (absent during war period).

*Amount Handled*—70 gm.

*Special Duties*—Gamma ray measuring.

*Visible Effects*—None.

*General Health*—Very good. Never been ill.

Date.....	3-28-21	5-20-21	7-27-21	9-30-21	11-29-21
R. B. C.....	4,980,000	5,080,000	4,810,000	5,730,000	5,790,000
W. B. C.....	3,800	5,000	5,050	4,200	5,800
Poly.....	48%	68%	44%	54%	64%
S. L.....	10		26	16	22
L. L.....	40	32	28	24	12
Trans.....			1	4	2
Baso.....	2		1	2	
Eosin.....					
Hemo.....				97%	85%

"No. 4 showed a constant leukopenia, and a relative lymphocytosis. No. 5 was normal, yet had been in service eight years, working at gamma ray measuring and tracing lost radium, and suffered with effect on fingers, (not progressive since radium is handled with instruments), yet the blood remained normal. Nos. 6 and 7 remained normal. No. 8 showed a relative decrease in polynuclears, and an increase in lymphocytes."

*Male*—Age 41—Single.

# RADIUM

165

*Continuous Service*—1 year.

*Special Duties*—Emanation measuring (samples).

*Amount Handled*—Cannot estimate.

*Visible Effects*—None.

*General Health*—Good.

Date.....	3-28-21	4-25-21	7-27-21	9-30-21	11-29-21
R. B. C.....	4,980,000	4,380,000	4,390,000	4,560,000	4,610,000
W. B. C.....	9,200	5,650	6,430	7,000	4,450
Poly.....	40%	32%	50%	40%	.....
S. L.....	8	16	6	18	.....
L. L.....	52	50	42	40	.....
Trans.....	.....	2	2	.....	.....
Baso.....	.....	.....	.....	2	.....
Eosin.....	.....	.....	.....	.....	.....
Hemo.....	.....	.....	.....	90%	82%

"No. 14 and 17 showed similar conditions. No. 17 was a stenographer and received only short exposures to large amounts of radium. No. 18 showed a marked leukopenia, and a relative lymphocytosis, and yet was only the porter, handled no radium, and his general health was good.

*Male*—Age 29—Married—4 children prior to radium work.

*Continuous Service*—6 months.

*Special Duties*—Porter of laboratories.

*Amount Handled*—None.

*General Health*—Good.

R. B. C.	W. B. C.	Poly.	S. L.
6,210,000	3,450	34	14
L. L.	Baso.	Myelo.	Eosin.
36	2	—	12
Trans.			Hemo.
2			92%

"Unfortunately none of these reports were accompanied by the dental films carried for two weeks."

*"Dental Film Values.*—In order to form some idea of the relative amount of exposure that each worker got, I requested that each carry a dental film for two weeks. To get gradation values, I took the time necessary to produce an erythema dose which with one of my machines requires four minutes (240 seconds) at 8-in. with a 9-in. spark gap and 5 ma. through 2 mm. Al filter. At 80-in. distance, this time becomes twenty-four hundred seconds, according to the law of inverse squares. At this distance, exposure of ten of the standard (Eastman) dental films from ten up to one hundred seconds will show ten gradations from the faintest shadow to the darkest shade possible. Each of these shades will then measure from  $\frac{1}{2,400}$  to  $\frac{10}{2,400}$  of an erythema dose. In my own institute, of the 10 workers two who handled the radium and x-rays most, clinically, received in two weeks about  $\frac{1}{2,400}$  of an erythema dose."

The majority of the films sent in showed no more, but many were entirely black; and since the film will only record a certain maximum shade of blackness, these people are probably dangerously exposed. I would suggest that any one whose film, carried for two weeks, shows definite blackening, should increase the protection. This makes a simple practical test, which will give warning long before changes in the blood can be noted."



## RADIUM

"Among the other blanks returned were those of 175 physicians, 55 nurses, 62 technicians, 25 stenographers, and 16 general assistants. The stenographers were all normal, or at least had no symptoms or blood changes to suggest radiation effect. Therefore, the general radiation effect in our American laboratories can be ignored."

"I found that the nurses, technicians, and general assistants all did more or less radiological work, and can therefore be classed together (159). Of this group there were only 10 which showed any abnormal symptoms, or blood change, or excessive exposure on the dental films. One of these showed 53 per cent lymphocytes, 38 per cent polymorphonuclears, and about 6,000 total leucocytes."

One of the correspondents remarks: "I am very well generally, much better in many ways than when I began x-ray work; but most of the time, after I leave the work for the day, I find myself completely exhausted, and it requires about nine hours' sleep to put me in good condition again. A peculiar thing about this feeling of exhaustion is, I do not notice it while around the x-rays. (She is supposed to have had Bright's disease preceding x-ray work.) She worked five and one-half days, five hours, at roentgenotherapy, for five and one-half years. Her blood was normal. Her film showed about  $\frac{5}{2,400}$  of an erythema dose. One nurse noticed menstrual irregularity. Several showed an excess of exposure on the dental films."

The physicians showed most change, as might be expected. They do the fluoroscopic work, and most of the radium and roentgenotherapy. In general, they have been doing radiation work over a longer period and working more intensely. Those who work with radium or with the high voltage x-ray machines, showed an excess exposure on the dental films. I would therefore urge that these workers increase their protection until they can carry a dental film (face outward) for two weeks with little or no fogging."

"The blood studies, if reduced to averages, would undoubtedly come entirely within the normal limits. In general there is a tendency to a reduction in leucocytes, and a relative increase in lymphocytes, with a marked increase in eosinophiles, in a few cases. In most instances, these changes are only slightly beyond the normal limits, but when taken with similar observations made by other authors, even though on a smaller scale, they are probably significant of excessive radiation and should be interpreted as danger signals."

"The five worst blood records sent to me were as follows:

Total erythrocytes ....	4,900,000	5,080,000	5,140,000	5,210,000	4,600,000
Total leucocytes .....	5,900	4,400	8,100	7,200	6,600
Hemoglobin .....	95%	80%	100%	94	103
Differential leucocyte count:					
Small lymphocytes .	31	42	42	39	45
Large lymphocytes .	14	7	1	8	....
Transitionals .....	5	1	1	0	2.5
Polymorphonuclear..	42	48	52.5	52	49
Eosinophiles .....	8	2	3	0	2
Basophiles .....			5	1	1

"All these have occurred in physicians who have been at the work only a comparatively short time. Four of the five had black dental

films. The fifth had only a faint fog on his dental film. These blood changes may be caused by some other conditions than radiation, but if due to radiation, then we must conclude that some of the younger men are not giving as much attention to protection as are the older workers. It is indeed surprising to find the blood of the older radiologists in such good condition."

*"The Blood-Clotting Time.*—Accepting three to five minutes as the normal, there were only twelve reports of abnormal clotting time. These were respectively, 10, 7, 7, 9, 14½, 7½, 9½, 10, 7, 5, 7, 7, or a delayed clotting time in 3½ per cent. There was no abnormally rapid clotting reported. The one who had a nine minute clotting time had an eosinophilia of 12 per cent, for which he could give no cause. In other respects his general health and his blood were normal. The one who had a clotting time of fourteen and one-half minutes, had a systolic blood pressure 11 points below normal, but in all other respects he seemed to be normal."

*"Blood-Pressure.*—Accepting 120 mm. as normal for the age of twenty years, and adding 1 mm. for each two years above twenty as normal, there has been a general decrease in the systolic blood pressure. This has been the most constant abnormality found in these studies. The reduction varied from 5 to 38 points. In general there has been a reduction in systolic pressure of 10 to 15 points below normal. In only one marked case was there associated abnormal blood. In this one there was a 44 per cent lymphocytosis, and a 50 per cent polynuclear count, while the total leucocytes were 8,120. The low blood-pressure is too common to be ignored, but I believe that it is not caused by the radiation, because there are no other radiation effects corresponding, and it does not bear any relation to the amount of exposure, or the duration of service. It is most likely caused by the high tension electric effects."

*General Symptoms.*—Only 11 out of 338 report any general symptoms which they attribute to, or which seem to be associated with, the occupation. This, it seems to me, is a fair percentage of health, and should not lead a diagnostician to attach great importance to the occupation as an etiological factor in general symptoms."

"Sinusitis is reported by two. One simply says that "the ozone from treatments irritates." The second reports "a steadily advancing pansinusitis (pyogenic) and a steadily decreasing resistance, sixteen carbuncles in 1920, thirteen abscesses in 1921, with loss of 'pep.' From a health viewpoint, I was considered A No. 1, until 1916—three years after entering x-ray work." Since then he has had several sinus operations and has quit x-ray work. He is recovering. It would seem unwise to attach much importance to the radiation in this case, since similar cases are not uncommon in people who are in no way exposed to the rays."

"One radiologist reports as follows: Four years ago, when commonly handling 500 mg. of radium, with lack of precautions, such as standing three to four hours daily near radium, unprotected, I found myself running an extremely low systolic B.P. 100 to 105. Three months later I developed what was diagnosed as degenerative changes in the heart wall. With this there came rapidly structural changes in the liver, phlebitis of severe type affecting both lower extremities. After treatment for six months I returned to guarded radium application, with complete recovery from all symptoms, including the myocardial. Blood R. 5,100,000; W. 8,700; H. 85."

## RADIUM

*"Conclusions.—1.—Undue exposure to the x-rays or radium is associated at times with a moderate leukopenia, a relative lymphocytosis, a relative polycythemia, and occasionally an eosinophilia."*

*2.—A low blood-pressure is quite common in radiological workers, which does not seem to be associated with any other definite symptoms."*

*"3.—The asthenia, sometimes noted, can probably be accounted for by strenuous work, caused by the great interest and also by the desire to meet the heavy "overhead" charges which must be carried by the radiologist. These symptoms are also probably caused by close confinement, lack of fresh air, and lack of recreation."*

*"4.—The skin changes found in the earlier workers are not increasing, and are being avoided entirely by the younger ones, because of the increased knowledge, and increased protection."*

*"5.—Complete protection can undoubtedly be obtained. It requires not only the means, but the continual caution on the part of the individual."*

*"6.—Increased protection is needed by those who are working with the gamma rays, or with the higher voltage x-rays."*

*"7.—A dental film carried in the pocket for two weeks, will give a quick index of excessive exposure. If definitely fogged or blackened, protection should be increased."*

*"8.—Shortening the hours of work, and increasing the amount of fresh air and recreation will probably remove symptoms, and prevent future trouble."*

\* \* \* \* \*

Burton J. Lee, M.D. (New York City). Treatment of Recurrent Inoperable Carcinoma of Breast by Radium and Roentgen-Ray. Jour. Am. Med. Assn. lxxxix, 1574-1576, Nov. 4, 1922.

*"All cases of carcinoma of the breast may be classified in one of five clinical groups, (1) primary operable; (2) primary inoperable; (3) recurrent operable; (4) recurrent inoperable, and the (5) prophylactic group, the last comprising patients referred to us following radical operation of the breast for prophylactic irradiation, there being no obvious evidence of cancerous disease at the time of their admission."*

*"The present paper is a study of recurrent mammary cancer treated in the breast clinic at the Memorial Hospital during the years 1918, 1919 and 1920, comprising a series of 218 patients, practically all of whom have been completely followed up to the present date."*

*"We have included none from the 1921 group, as sufficient time has not elapsed to warrant reporting the results of treatment. The object of this paper is to determine whether or not radiologic treatment of recurrent carcinoma of the breast is justified by the results obtained in this clinic."*

*"Most of the recurrent cases were inoperable at the time of their admission to the clinic. In the recurrent breast group, only six patients have presented themselves, in the years 1918, 1919 and 1920, who could fairly be classed as having operable cases. A small, nonadherent skin lesion, or a small movable node, low down in the axilla, may properly be considered operable, if no other evidence of disease is to be found. Under these circumstances it is a correct procedure to excise the recurrent nodule, irradiation being given both before and after operation. With the presence of several such lesions, however, one must conclude that the disease is probably widely disseminated, and any thought of any*



operative relief must be discarded. In this event, irradiation is the type of therapy that must be relied on."

"A considerable number of cases, namely, ninety-four, were so far advanced at the time of admission that they were obviously hopeless from the outset. The very advanced breast recurrences must be set apart from those cases in which a reasonable palliation, if not a considerable regression of the disease, may be expected. All that one may hope to accomplish for those patients with a far-advanced lesion is a relief of their suffering by adequate amounts of codein or morphin; frequent dressings when foul ulcers are present, and perhaps at times sufficient to satisfy the mind of the patient that treatment is still in progress. If we therefore exclude these patients from the whole number of 218 cases, we have remaining 124 patients in whom irradiation as a therapeutic agent could be determined with a fair hope of some favorable result."

*"The Prevention of Recurrence; Proper Selection of Cases.*—In the recent rapid development of therapy by roentgen-ray and radium the surgeon has at times seemed unwilling to relinquish anything in the surgical treatment of cancerous disease. The presence of a carcinoma in a breast is not necessarily an indication for a radical amputation, for a careful physical examination of the patient may reveal some factors which would militate against success by operation. The cases treated surgically must therefore be well chosen if the percentage of recurrence is to be kept at a minimum."

*"Preoperative Irradiation.*—It has been the practice at the Memorial Hospital for several years to give a preoperative cycle of roentgen ray in every case of carcinoma of the breast before submitting the patient to operation. As a rule, a period of from seven to ten days is allowed to elapse, between the time of the last irradiation and the day of operation. We believe that the preoperative cycle is of great service in forestalling recurrence, but up to the present time a sufficient number of cases has not been accumulated to furnish a proper comparison with groups of patients in other clinics where the preoperative use of the roentgen-ray has been omitted; eventually such a study will unquestionably furnish a proper estimate of the real value of preoperative treatment. In the vast majority of cases we have seen no evidence which would lead us to believe that the preoperative cycle interferes materially with wound healing, or adds to the liability of wound infection."

*"Postoperative Irradiation.*—From two to three weeks following operation, every patient is subjected to a postoperative series of roentgen-ray treatment over the whole breast and drainage areas. An interval of from six weeks to two months is then allowed to elapse, when a second similar cycle is administered. Sufficient data have already been accumulated at the hospital to make one feel very certain that postoperative treatment prevents certain recurrences and postpones the appearance of practically all recurrences. In addition, it unquestionably prolongs the life of the patient. We feel, therefore, that postoperative irradiation has proved its worth without any reservation."

*"Results of Treatment.*—One may well ask what the average expectation of life is from the time of the first appearance of a recurrent breast tumor without any irradiation. Such a question might imply that all breast cancers are of the same pathologic type and follow a similar

## RADIUM

clinical course. We know that this is not the case. At present, with the co-operation of Dr. James Ewing, pathologist at the Memorial Hospital, we are engaged in an effort to classify more satisfactorily the various types of carcinoma from a pathologic point of view and to study their reaction to various forms of irradiation. A papillary adenocarcinoma, a tumor well known to be of low-grade malignancy, will certainly permit a long period of life following recurrence than a rapidly growing cellular tumor. Similarly, a fibrocarcinoma in a woman of 70 may be expected to grow with much less rapidity following reappearance of the disease than a fulminating recurrence complicating pregnancy in a young woman. Nevertheless a gross clinical judgment as to the value of irradiation as a means of treatment for recurrence may be reached if we compare results giving the duration of life from the appearance of recurrence in nonirradiated and irradiated patients."

"At the New York Hospital, in the First Surgical Division, where, through the courtesy of Dr. Charles L. Gibson, I was able to follow the breast cases especially, the length of life after recurrence in a series of twenty-two patients on whom a radical amputation had been performed, with no subsequent irradiation, was six and a half months. In the patients in the present series, who have been treated by irradiation following the appearance of recurrence, the length of life after recurrence has been two years and four months, a decided advantage, as one may readily see, in favor of irradiation."

"Of the total of the 124 patients in whom some favorable results from irradiation might be expected, thirty-one are alive at the writing of this report, which is 25 per cent. of the total number. Of the thirty-one patient, twenty-two are doing well, while nine are doing badly. A brief table is given, that the data may be more readily available."

"In general, the more cellular the tumor, the better the response to treatment by irradiation. The younger the woman and the more rapid the recurrence, the poorer is the result to be expected from irradiation."

### RESULTS IN THIRTY-ONE CASES

Case	Operation to Recurrence		Recurrence to Date		Total Duration After Operation	
	Years	Months	Years	Months	Years	Months
PATIENTS DOING WELL						
1.....	..	6	3	8	4	2
2.....	13	..	6	..	19	..
3.....	..	7	4	10	5	5
4.....	..	3	6	4	6	7
5.....	..	3	4	8	4	11
6.....	..	2	3	..	5	..
7.....	2	3	3	5	5	8
8.....	..	1	2	9	2	10
9.....	..	..	3	2	3	2
10.....	2	..	2	10	4	10
11.....	..	3	1	8	1	11
12.....	..	..	2	..	2	..
13.....	..	1	2	2	2	3
14.....	1	..	1	6	2	6
15.....	..	9	1	7	2	4
16.....	7	1	2	4	9	5

Case	Operation to Recurrence		Recurrence to Date		Total Duration After Operation	
	Years	Months	Years	Months	Years	Months
PATIENTS DOING WELL						
17.....	2	..	1	8	1	10
18.....	1	1	2	2	3	3
19.....	1	7	1	11	3	8
20.....	8	..	1	10	2	6
21.....	6	4	2	2	8	6
22.....	10	..	1	10	2	4

## PATIENTS DOING BADLY

23.....	..	3	5	..	5	3
24.....	1	1	3	..	4	6
25.....	1	..	3	8	4	8
26.....	..	..	2	10	2	10
27.....	..	11	4	9	5	8
28.....	1	6	3	6	5	..
29.....	..	6	2	3	2	9
30.....	4	..	2	7	6	7
31.....	3	..	2	3	5	3

*"Types Best Suited for Irradiation by Radium.*—Small localized lesions in the infraclavicular region, or adherent to or involving the chest wall, small localized skin metastases or small accessible nodes are most amenable to treatment by radium itself."

"Some of our best results following the use of radium in the recurrent group have been in the infraclavicular region. In some of these cases, applications of a radium pack have resulted in a complete disappearance of the growth. One of the patients has now gone one and a half years with no further evidence of disease to be made out. The details of radium therapy and the methods employed have been fully described in a recent article, and will not be described here."

*"Types Best Treated by the Roentgen Ray.*—Recurrences best treated by the roentgen-ray include diffuse cutaneous involvement, examples of so-called inflammatory carcinoma, extensive involvement of nodes in the axillary or supraclavicular regions, and mediastinal of pleural metastases, as well as bony metastases, in various parts of the body. The technic employed has been fully described in a recent paper. At present we are still depending mainly on the old type of roentgen-ray machine, and have been reasonably satisfied with the results obtained. Some of the most striking effects have been seen in the treatment of diffuse cutaneous involvements, an area of considerable disease disappearing in a few weeks under appropriate irradiation, leaving an apparently normal skin. In some of these cases, a later examination showed a reappearance of the lesion."

"The new 200,000 volt machine now in operation is being used on carefully chosen patients, but sufficient time has not elapsed to make any report on this method of therapy. We are very hopeful that some of the mediastinal and pleural extensions of the disease may yield some encouraging results by this new method of treatment."

"The gross and microscopic effects of the treatment of cancerous



## RADIUM

diseases by radium and the roentgen-ray have been described elsewhere."

"*Conclusions*—1. As a prophylaxis against the recurrence of breast carcinoma, a careful selection of patients for operation must be made."

"2. Preoperative and postoperative cycles of roentgen-ray are important prophylactic measures against recurrence."

"3. A follow-up in every patient with carcinoma of the breast operated on should be adopted as a routine. No surgeon should operate on a patient with breast cancer without appreciating that an integral part of the procedure is following up the patient, with the idea in view of discovering the appearance of metastases at an early date, permitting the application of irradiation as soon as possible."

"4. Properly applied irradiation to recurrent breast carcinoma definitely prolongs the life of the patient."

"5. I believe that ultimately, with more complete knowledge and better technic, a still further control of the recurrent phase of this disease may be expected."

\* \* \* \* \*

Arthur Burrows, M.D. (Manchester, The Radium Institute). A British Medical Association Lecture on the Problem of the Radium Therapy of Cancer. *British Med. Jour.*, 33-34, July 8, 1922.

"A few facts have been established in respect to the action of radium on cancer cells during the last twenty years. The first is that cancer cells can be destroyed by rays, but this statement is modified by the knowledge that, given a sufficient dose, practically all tissue cells can be killed by radiation, and so arises the second point—namely, that there is a minimum dose which will just kill a cancer cell and will not, as a rule, kill an ordinary tissue cell. This is called the "minimum lethal dose," the "lethal dose," or the "cancer dose." This lethal dose varies with different tumors and different conditions."

"Theoretically, given a known quantity of rays, the lethal dose of the cells of a certain cancer, and the size and situation of the tumor to be treated, it is possible to destroy almost any cancer, but unfortunately all these three conditions are variable and are made up of variables. Thus, with regard to rays, the beta rays from radium are not uniform, but are made up of groups of rays which are of different penetrability. Similarly the gamma rays are mixed, as also are x-rays. Beta rays can be screened off entirely by using metal plates of a definite thickness, or they may be partially cut off by using thinner or less dense material. It is very difficult to cut off all gamma rays, but certain of them can be eliminated by a process of screening and an attempt made to obtain rays of a certain minimum penetrating power. In the same way by screening and by improving and standardizing apparatus an attempt is made to keep x-rays as constant as possible, but unfortunately it is not known exactly what is the right type of ray for each tumor. A few facts are known—for example, that a rodent ulcer will do well with unscreened radium (that is, mostly beta ray treatment), but gamma ray treatment is also effective. I think, however, that if beta rays fail in the treatment of a rodent ulcer gamma rays will rarely be successful. Skin diseases are obviously most suited for rays of a longer wave-length. Most rays seem to affect lymphosarcomata, while carcinoma of the tongue as a rule yields best locally to beta rays, but of course with beta rays there is a strong caustic or destructive action. One of the claims of the Erlangen x-ray treatment is that a correct ray for the destruction of carcinoma

of the cervix of the uterus has been established. But the size, density and depth of a tumor obviously affect not only the quantity of rays penetrating the whole of a growth—for that can be rectified—but also the quality, which cannot be thus adjusted when radiation is being applied from a distance. The actual insertion of a varying number of suitably screened radium tubes into a tumor is the only method of insuring uniformity in the quality of the radiation applied. Some tumors are not suitable for the burying of tubes in their substance, and it is then seen how complicated the whole subject is, and how the question of the quality of the rays used, and the dosage, merge into a consideration of the size, density, nature and position of a tumor."

*"Lethal Dose.* Assuming that beta rays are used to kill a cancer cell, it is probable that the lethal dose for these would be different from the lethal dose for gamma rays; or, pushing the matter farther, the lethal dose of soft x-rays would be different from the lethal dose of hard x-rays, as the destructive action of radiations must depend on the quantities of them which are actually stopped in the cells of a growth. Therefore, in fixing lethal dose for a certain tumor, it must be established for a definite type of ray, and this does not in practical therapy depend altogether upon the operator, but upon the size, nature and position of the growth he has to radiate. Thus, change the position of the growth by one centimetre and it may be necessary to alter the type of ray used, and with that the dosage if raying is being carried on from a distance. Then, again, the lethal dose for a tumor may be very near that of the ordinary tissues, and a very fine or no margin left between the quantity and type of rays destroying the normal tissue and the cells of the tumor."

"As an example of this last possibility the secondary nodule which may be present on the chest wall following an amputation of the breast may be given. Over this may be stretched a thin and delicate covering of epithelium, and any application of rays given to the nodule may destroy the skin beyond repair long before the tumor cells in the nodule itself are killed."

*"Nature of the Tumor.* It is an established fact that some tumors are destroyed by rays more easily than others—for example, a small round-celled sarcoma is more easily caused to disappear by irradiation than a squamous-celled carcinoma; but absolute uniformity in respect to the behavior of groups of growths under radiation does not exist, as other factors, such as the patient's general resistance to tumor growth, or the situation of the tumor, alter its susceptibility to rays and possibly also the stage of development and age of the tumor itself. Is, for instance, a rodent ulcer growing in the skin a different growth from one growing in bone? The same treatment will not cure them both. In fact rodent ulcers of the skin are easily cured by radium; rodent ulcers invading bone are only exceptionally cured."

"Nor must the fact be forgotten that rays seem most markedly to affect the reproductive functions of cells. Therefore let the tumor grow quickly, and most often the local growth will rapidly diminish, and vice versa; but unfortunately the local tumor is not the only consideration, for growths such as encephaloid carcinoma of the breast, which grow very rapidly and respond well to radium, soon form secondary deposits, so that the ultimate result is not so good. Or again round-celled sarcomata are usually quoted as types of tumors which respond well to radium treatment, but the more slowly growing and diffi-

## RADIUM

cult to treat spindle-celled sarcomata with perseverance give the best results in the end."

*"Size and Density of Tumors."* The size of a tumor is important from several points of view. If a tumor is exceedingly large commonly there is a poor blood supply at the center (if it is a carcinoma), and there is a great tendency for the tumor to break down and slough under treatment, while at the same time a poor blood supply does not give adequate chance of repair following the treatment. Again, the size of the tumor has a marked effect upon the size of the dose of radiation which is given if an attempt is to be made to destroy all the cells it contains. A small tumor can fairly easily have an even radiation applied throughout its substance, but if it is very large, provided the rays are applied from one direction, the quantity falling on the near side of the tumor will be very much greater than that emerging from the far side. It is also apparent that the density of the growth will have a similar effect, for the denser the tumor the greater will be the difference between the entering and emerging rays."

"In the early days of radium treatment Wickham and Degrais suggested the method of cross-fire as one of the means of getting over this difficulty—for instance, if a tumor can be treated from two sides, all other factors being equal, double the dose can be given to the tumor by applying radium to it on those two sides. If the tumor is accessible it may be radiated from more than two sides. What is done by the Erlangen method of x-ray treatment is very much the same thing. In order to get a sufficient quantity of x-rays to the tumor, rays are directed through several different areas of skin towards the tumor, which areas are called "ports of entry." It is thus seen that the method is the same as the cross-fire system used by Wickham and Degrais."

"With radium and radium emanation treatment the difficulty is also partly met, as has already been mentioned, by burying radium or radium emanation in the growth, or by varying the distance of the applied radium from the external skin. In the foregoing reference to the size and density of a tumor it has been more or less assumed that the tumor has been regular in outline and of uniform density throughout. But in practice, of course, malignant growths are of many and varied shapes, and they have near and distant secondary deposits; also they are by no means of uniform density, so that the problem of dosage becomes very complicated, and the most that can be hoped for is to obtain an approximation to what is desired which will work in practice."

*"The Position of a Tumor."* Its position has a very similar influence to the size and density of a tumor upon its susceptibility to radiations. If, for instance, it lies beneath or in tissues such as muscle and bone, it may become almost impossible to give it adequate radiations from the surface. If such factors as these are not present it may be possible that radiations from one side where the tumor is nearer may, at least in part, make up for deficiencies in radiation from the other side from which the tumor is farther away; but to get a proper quantity of rays traversing the growth many ports of entry may have to be used, and it becomes very difficult to get absolute accuracy of dosage. When cancers invade or are adherent to certain structures and organs such as bone, the stomach, bowel, liver, or lungs, treatment is rendered much more difficult, and often at the present time fails to produce a good result. It seems that not only is the nature of the tumor an important factor in ray treatment, but also the nature of the tissue and organs that



it invades. The more accessible a growth is, as a rule, the better are the results, but growths of certain organs, such as the oesophagus, rectum and tongue, seem to resist radium treatment more than elsewhere."

"The consideration of the preservation of the skin is an ever-present problem to the radiologist. It has been already mentioned that under certain conditions it is possible that a stretched or ill-nourished skin may be more rapidly destroyed than a tumor, and, moreover, if the blood supply or ability of the skin to repair is bad, unless proper care is used the last condition may be worse than the first, from the formation of an intractable ulcer—not an x-ray or radium ulcer but a malignant one. That is to say, it may not be possible to give a suitable destructive dose to the ill-nourished tissues without risk. If one could be sure of destroying such a malignant growth beneath the skin there would be less difficulty in dealing with the factor of the skin, for it is almost certain that scar tissue would eventually form and fill up the gap; but the uncertainty of destroying the growth under these conditions makes the radiologist take more care in endeavoring to preserve the skin, and hence has arisen the so-called "erythema dose." The burying of radium tubes will often, but not always, obviate this difficulty. In the case of rodent ulcers and epitheliomata of the skin not invading bone or cartilage, the skin, as a rule, has been modified or destroyed by the growth. In such cases the preservation of the epithelium need not be considered and marked local destruction produced if necessary, with knowledge that good repair will take place afterwards and a soft, supple scar be formed."

"It will be seen from the foregoing remarks that the whole system of ray treatment is exceedingly complicated. The difficulties of a dosage are modified by nearly all the usual things which may take place in a tumor from its nature or position. The possibility of actually stimulating an outlying portion of a growth which has been only partially radiated must always be borne in mind, although it is not as a rule a difficult problem in practice, because fortunately the range of dosage producing stimulation is an exceedingly small one."

"What is needed is a large number of physical measurements of the different parts of the human body and of pathological growths, and a full and complete investigation of the nature of the lethal dose for cancer cells; when these have been made an approximate idea may be obtained of the method of treating tumors in different situations, although even then it seems that a number of imponderable biological problems, such as the resistance of the organism as a whole and the resistance of tissues locally to cancer growth, remain to be solved."

"But in spite of all these difficulties and the disadvantageous position in which radiologists are placed in this country of treating practically only inoperable cases, many good results are obtained from radium treatment:  $7\frac{1}{2}$  per cent. of all the cancer cases (mostly inoperable) which come to Manchester for radium treatment are alive and well today after periods varying from two to seven years, and many cases of carcinoma of the cervix of the uterus, breast, skin, lip and other regions are in perfect health who would but for radium be dead; while endothelioma of the parotid gland and spindle celled sarcomata show still more gratifying results. Moreover, short of cure much valuable palliative work is done, while in non-malignant conditions, such as exophthalmic goitre, Hodgkin's disease (when young), keloid, cavernous and capillary naevi, the percentage of cures is high; finally, radium is specific for excessive uterine hæmorrhage and spring catarrh."

## **RADIUM**

### **AMERICAN RADIUM SOCIETY.**

The eighth annual meeting of the American Radium Society was held in San Francisco June 25 and 26 under the presidency of Dr. R. E. Loucks, of Detroit. The local committee on arrangements was composed of Dr. Howard Morrow, chairman; Dr. William Montgomery and Dr. Laurence Taussig. During the scientific session the following papers were presented: Certain Biological Principles of Radiation Therapy, by Dr. Sanford Withers; the Changes in the Carcinoma Cells of Cervical Cancers Caused by Measured Radiation Doses, by Dr. Henry Schmitz; Radiation Therapy in Diseases of the Uterus, by Dr. John M. Lee; Radiation Therapy in Bleeding Uteri, by Dr. Harry E. Bundy; Radium and Roentgen Therapy in the Treatment of Carcinoma of the Thyroid, by Dr. H. H. Bowing; Indications and Technique of the Irradiation Treatment of Esophageal Carcinoma, by Dr. James T. Case; the Use of Radium in the Treatment of the Leukemias and Hodgkin's Diseases, by Dr. W. H. B. Aikins; the Use of Radium in Apparently Hopeless Cases, by Dr. Emil G. Beck; Epithelioma of the Lip, by Dr. T. C. Kennedy; Radium Treatment of Vascular Nevi, by Drs. Howard Morrow and L. R. Taussig. On Tuesday afternoon a radium clinic was held at the University of California Hospital. On the evening of June 25, the annual dinner of the society was held, at which time Dr. Loucks gave the presidential address on Radium Treatment of Toxic Thyroid with Metabolic Deductions.

---

### **AMERICAN COLLEGE OF RADIOLOGY.**

The American College of Radiology was organized in San Francisco during the last meeting of the American Medical Association and the following officers were elected for the first year. Dr. George E. Pfahler, Philadelphia, president; Dr. Wm. H. Stewart, New York, president-elect; Dr. Henry Schmitz, Chicago, vice president; Dr. Albert Soiland, Los Angeles, executive-secretary.

The purpose of the organization is to elevate the standards of radiology to the highest plane. The membership will be practically limited to one hundred physicians who are now members of the American Radium Society, American Roentgen Ray Society, Radiological Society of North America, Canadian Radiological Society or societies of equal standing in North America.

---



---

---

# STANDARD CHEMICAL COMPANY

---

---

PIONEER AMERICAN  
PRODUCER OF  
RADIUM

---

---

GENERAL OFFICES

FORBES STREET AND MEYRAN AVENUE

PITTSBURGH, PA.

---

---



# RADIUM

STANDARD CHEMICAL CO.

*"Know the Company from Which You Buy"*

## AN IMPORTANT POINT IN OUR SERVICE

In our monthly Courses of Lectures at Pittsburgh, two entire days (preceding the lectures on radium-therapy) are devoted to a comprehensive presentation of the fundamentals of the physics of radioactivity as these relate to the therapeutic use of radium.

Some of the important topics covered are:

1. The nature of radioactivity.
2. The nature of alpha, beta and gamma rays.
3. A dark-room demonstration of the properties of the rays.
4. The absorption of the rays in matter, and the effects of distance, cross-fire and implantation on ray intensity.

The user of radium should not underestimate the importance of a proper understanding of the physics of radioactivity.

**RADIUM CHEMICAL CO.**  
PITTSBURGH, PA.

NEW YORK

BOSTON

CHICAGO

SAN FRANCISCO

DALLAS